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THE FUNCTIONS OF THE FULL TIME PATHOLOGIST IN HOSPITALS

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JERSEY CITY, N. J.

The functions of the pathologist are but vaguely defined and understood. Since Virchow's first pathologic publications, about seventy-five years ago, the progress of medicine in general has been rapid. With this the functions of the pathologist have increased in scope and importance.

After the fundamental work of the great German pathologists Virchow and Cohnheim, pathologic anatomy was separated as a distinct branch of medical science. At first the pathologist, as "prosector," had a narrower field, confined mainly to the study of autopsy material. The rapidly progressing surgery, however, opened a new field of surgical pathology, thereby aiding the study of disease in vivo. The general advances of medicine at the same time made the pathologist an important adjunct in all lines of diagnostic work. This practical standpoint of diagnosis is responsible for increasing the importance of the laboratories beyond the scope of morphology. All branches of so-called clinical pathology (biochemistry, bacteriology, serology, hematology, animal experimentation) made rapid progress in developing diagnostic methods and have increased the usefulness of the pathologist as a diagnostician.

Such considerations are mainly responsible for the fact that the laboratories and the pathologist play an important rôle in the standardization of hospitals. Briefly expressed, the hospitals have the following functions: (1) to take care of patients, (2) to promote medical progress and (3) to elevate the educational standards of the medical profession. To comply with such requirements, the laboratories and the pathologist have a great responsibility. The important rôle of the pathologist is best defined by discussion of the following four functions: (1) as laboratory consultant, (2) as research consultant, (3) as scientific administrator and (4) as educational director.

LABORATORY CONSULTANT

The size and organization of the laboratories depends on the type and size of the hospital and on many other factors. The various branches of histopathology and clinical pathology require more or less technical personnel. These in turn need supervision and direction. This must be supplied by at least one physician-pathologist. This pathologist is the laboratory director and as such is necessarily the link between clinical and laboratory medicine. While even routine work, to constitute worth while relationship to clinical diagnosis, requires the special training of the biochemist and bacteriologist, the really proper field of the pathologist is tissue pathology.

In the first place the pathologist is responsible for the autopsy work. Only too often there are two indications for autopsy work in the hospitals: (1) the requirement of autopsies in not less than 15 per cent of deaths, for intern training; (2) to check the clinical diagnosis and determine the immediate cause of death. As a matter of fact, autopsy material offers a veritable treasure mine of medical knowledge. There will be a natural increase in the percentage of autopsies obtained if the value and use of the autopsies are demonstrated to the attending and resident staffs.

Remarks such as "What's the use of the autopsy, we know the patient had pneumonia" are quite common. The patient may have died of pneumonia but there may be, besides the various scientific aspects of this condition, a great many striking abnormalities in the other organs which are most instructive, demonstrating various phases of pathogenesis of many other diseases (coronary sclerosis and so on). Frequently autopsies are mistakenly limited to confirmation of the clinical diagnosis. Common remarks by clinicians or residents are also "We are interested only in the gallbladder and liver" or "We do not care about the heart or brain." As a matter of fact the real results of the autopsies can be seen only after the coordination of all the gross and microscopic observations. Besides the vast pathologic aspect, the autopsies offer opportunity for normal anatomic, bacteriologic and surgical studies.

At this point emphasis has to be laid also on the technic and plan of autopsy work, not only for the success of scientific studies but to avoid justified antagonism on the part of the lay public and undertakers. Often utilization of autopsy work is limited to gross observations instead of extending it to various degrees of histologic studies. Various phases of this work have to be recorded by means of photomicrography, drawings and lantern slides. Such records are important not only as part of the hospital work but also from the standpoint of educational research and legal medicine. Gross and microscopic materials have great value as teaching material when used for meetings, demonstrations and permanent museum work. If properly studied and worked up, such material also suggests further experimental work. Surgical pathology is often also appreciated only so far as surgical diagnosis goes. The fact, however, is that surgical pathology affords opportunity to study various phases of the pathogenesis and course of diseases in vivo rather than the terminal

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stages of autopsy observations. It offers the most stimulating teaching material not only for the education of the staff but also for the pathologist himself. It is granted, however, in regard to surgical pathology, that diagnostic work is of prime importance from the standpoint of the patient so far as prognosis and further treatment is concerned.

The judicious use of the frozen section method is helpful, but rapidity of diagnosis should not be emphasized at the expense of accuracy. Medicolegal questions not only necessitate accurate pathologic records but often require toxicologic examinations. Study of diseases naturally embraces pathology, bacteriology, serology, immunology and hematology in the closest coordination. For many routine examinations along these lines, technicians are relied on entirely. It is obvious that the methods of the technicians should be supervised by superior knowledge, which requires special training of the highest quality. This is best exemplified in relation to biochemistry. Many of the methods in blood chemistry (for example, urea determination by the Marshall method) are so simplified and standardized that technicians are capable of doing them, but no matter how simple any of them are the sources of error are innumerable. The greatest attention has to be paid to standards, which deteriorate in shorter or longer time and, even if new, require careful checking. Standardization and calibration need competent supervision. Most of the methods, moreover, require judicious adaptation. No technician would be expected to decide, for example, what kidney or liver function tests are generally reliable or most suited for certain clinical cases.

TABLE 1.—*Laboratory Consultant*

I. Acquaintance of standard laboratory methods:
   1. Gross morphology (autopsy, surgical pathology, embryology)
   2. Histologic technic (special tissue stains)
   3. Bacteriologic methods
   4. Serologic and immunologic methods
   5. Biochemical methods
   6. Hematologic methods
   7. Medicolegal, toxicologic methods
   8. Biologic methods (Aschheim-Zondek test, other animal inoculations)
II. Interpretation of laboratory methods by pathologist as diagnostician; initiation of methods as consultant
III. Adaptation, modification, of new methods

Finally, the pathologist will be called on to make interpretation of the results of laboratory examinations. His services are particularly helpful when consulted as to the choice of laboratory methods needed to build up the diagnosis. The necessity of adaptation and modification of new methods will be usually judged by the pathologist but often requires the highest skill, training and experience in the special lines (biochemistry, bacteriology and the like).

RESEARCH CONSULTANT

The pathologist is expected to be broadly trained in his knowledge of diseases; his knowledge must supplement that of the clinician; he must be able to correlate pathology and clinical medicine; he must know theories of pathogenesis and facts of prognosis; he must know the limits of certainty and the needs of future research. If all these things are true of him, he becomes thereby the most valuable of clinical and research consultants. For such scholarly attainment he has mainly two sources: (1) the practical study of material offered in the laboratory not only for diagnosis but also for self education; (2) literary studies. A reference library is indispensable not only for the pathologist himself but also for the entire staff, and his advice is often sought. To follow foreign literature, knowledge of languages is of great importance in literary research.

As the pathologist has to be engaged in continuous studies of the current literature, it is essential that the library should be kept up to date. He needs and obtains much stimulation by personal contact with various scientific societies. In this way he brings to his associates knowledge gained from sources and views not ordinarily within reach of the clinicians. He is not only expected to follow the progress of new medical developments but to be capable of contributing to these developments himself by utilizing his own observations. Original observations may be based on morphologic studies or may be clinical, in which case the pathologist may serve as adviser or consultant. Clinicians and pathologists may also join as collaborators in such original work as involves laboratory and clinical methods.

In experimental work with animals the pathologist has to possess a great deal of special information concerning the type of animals, their anatomy, pathology and so on. The value of such animal experiments will depend on the knowledge, experience and judgment of the pathologist in regard to methods, results and their interpretations.

Following all the work of the various branches of the laboratories, the pathologist gains knowledge of practically the entire scientific material of the hospital. He is thereby in the best position to suggest problems to be worked up or subjects to be published. Of course, it is granted that the scientific material is available only if it has been systematically collected and arranged (museum, index of diseases, collection of lantern slides, photographs, drawings).

The pathologist is a useful consultant and critic in preparation of papers of the staff and offering material for even larger publications, as books.

TABLE 2.—*Research Consultant*

I. Literary information past and current (library, journals, languages)
II. Membership in and attendance at special societies.
III. Experimental pathology (anatomy and pathology of animals)
IV. Original research:
   (*a*) Literary (case, statistical studies)
   (*b*) Experimental
V. Scientific or research consultant of staff:
   (*a*) Initiating
   (*b*) Collaborating
VI. Editor of publications (illustrations)

SCIENTIFIC ADMINISTRATOR

As the chief full time scientist of the hospital, the pathologist is first of all a scientific consultant for the medical director or superintendent in scientific questions. His advice will be sought for in such scientific matters as records, mortality and hospital hygiene.

Hospital records, when completed, are great assets in a hospital. Records have to be built up as completely as possible not only with all the laboratory information but also with photographic illustrations and charts. Such records can afford a wealth of material for research work at a much later date. This may also acquire great importance from a legal standpoint and with systematic indexing can be the basis of accurate statistical studies.

The problems of hospital hygiene are too many to enumerate. The pathologist is obviously responsible for all questions in connection with the morgue. The periodic health examinations of the entire hospital

personnel should include laboratory work, throat cultures and stool cultures. Hospital planning and construction require special consideration from the standpoint of asepsis (operating room, operating material, nursery).

The question of epidemics is to be thought of from the standpoint of prevention as well as actual occurrence. Cases of contagious infections are often discovered in the laboratory.

The food supply requires the systematic supervision of the laboratory.

TABLE 3.—*Scientific Administrator*

I. Relation of pathologist to medical director or superintendent:
  1. Records (statistics, photographs)
  2. Hospital hygiene:
    (*a*) Morgue
    (*b*) Personnel:
      Nurses
      Employees
    (*c*) Asepsis:
      Operating room
      Operating material
      Nursery
    (*d*) Epidemics
    (*e*) Food supply (e. g., milk)
II. Relation of pathologist to attending staff:
  1. Liaison officer between clinical and laboratory medicine
  2. Research and diagnostic consultant for patients
  3. Collaborator of papers of staff for publications and meetings
III. Relation of pathologist to resident staff (supervising interns, curriculum besides laboratory training, and so on)

In the hospital organization the pathologist is in intimate contact with the attending and resident staff. He is the liaison officer between all branches of clinical and laboratory medicine. His various contacts are mentioned in other places of this paper, but emphasis has to be laid on his work in the operating room and on rounds, and also to his collaboration with the attending staff in all the research and diagnostic work and preparation of papers of the staff for publications and meetings. His relation to the resident staff is an intricate one. Besides the laboratory training during their curriculum, the resident staff is in continuous touch with the laboratory and under direct and indirect supervision of the pathologist. It would be a great loss to the efficiency of a hospital if the pathologist should be considered only as a "laboratory" man in charge of routine laboratory work. With all the work enumerated, the scientific advice of the pathologist has to have the weight of authority but should not be confused with executive authority of the head of the hospital.

EDUCATIONAL DIRECTOR

The laboratory has a share in the diagnosis of every hospital case. The laboratory material, whether it is purely morphologic (autopsies and surgical pathology) or from the other various branches of clinical pathology, lends itself for educational purposes. There is nothing more stimulating to medical thought than a well prepared clinical-pathologic presentation with definite laboratory data, including gross and microscopic material, roentgenograms and other clinical information. It provides a firm basis for discussion of diagnosis and treatment.

All this laboratory material, if properly worked up and collected, is available not merely for one occasion but permanently for demonstrations and systematic lectures. Gross pathologic material (from autopsies or surgery) is best preserved in a permanent museum. The microscopic work can be demonstrated by microprojections or with lantern slides and photomicrographs. When photography is not suitable for reproduction, drawings may be necessary. All this material, when properly collected and classified, may become useful for illustration of publications at a later date. The same applies to the material derived from the various branches of clinical pathology (gross and microscopic material, charts). Such work, first of all, adds to the education of the pathologist himself, continuously increasing his experience and improving his judgment. It serves similarly as a stimulus for the entire staff collectively and individually. Comparative studies of pathologic material and roentgenograms, of clinical, morphologic and chemical studies of various diseases (such as nephritis) are examples of the cooperation between the individual departments of the hospital and the laboratory.

For the practical education of interns and the resident staff, well organized laboratory work forms an indispensable and firm basis as a part of their hospital curriculum, and appreciation of the various uses of the laboratory should develop to the very end of their hospital service. The interns and resident staff play a major rôle in securing permission for autopsies. Enthusiastic cooperation can be obtained only by rewarding their troubles with demonstration of the value and use of the autopsies. The direct and indirect links between the interns and the laboratory are too many to enumerate.

The pathologist contributes in numerous capacities to the training of nurses. Both undergraduate and graduate nurses should know enough of the purpose and methods involved in common clinicolaboratory procedures to cooperate in handling patients properly to obtain the best results.

Although the hospital constitutes an educational center for its own medical staff, the profession of its vicinity has also a legitimate claim on it. It is again the pathologist, with his well arranged collections from all branches of laboratory material, who can be called on to arrange or participate in shorter or longer postgraduate instruction courses.

TABLE 4.—*Educational Director*

I. Collection of gross and microscopic specimens as well as material of the various branches of clinical pathology:
  1. Museum preparation of gross pathologic specimens
  2. Permanent collection of microscopic slides
  3. Collection of lantern slides:
    (*a*) Gross specimens
    (*b*) Microscopic material
    (*c*) Charts
  4. Drawings
II. Education of attending staff by preparing material for clinical-pathologic meetings
III. Education of resident staff:
  1. Laboratory part of curriculum
  2. General courses and demonstrations
IV. Teaching of nurses
V. Postgraduate teaching
  1. Special postgraduate courses
  2. Regular pathologic demonstrations
VI. Education of public (lectures, demonstrations)

As in large institutions there is a continuous flow of gross pathologic material (from autopsies and surgery), systematic pathologic demonstrations can be arranged by the pathologist for the hospital staff as well as for the outside profession all the year round.

Some problems of preventive medicine and public health (cancer, tuberculosis and other infectious diseases) can be coped with successfully only if every medical institution, with its pathologist and pathologic material, will be a permanent source of public enlightenment through lectures and demonstrations.

SUMMARY

All these may seem as a formidable array of functions. Still the possibilities for the pathologist are not nearly exhausted if he applies himself with wholehearted devotion to the service of the institution. Every phase of the hospital work is directly or indirectly and intimately connected with his work. Therefore, essential requirement of the pathologist is a tactful personality, as the harmonious cooperation of the entire hospital personnel is of prime importance for the success of the institution.

On the other hand, if the hospital wants to secure the benefit of the best services of the pathologist, it is under numerous obligations to him. First of all the pathologist has to have the authority and respect as the chief scientist of the institution. He is not only a man of special training but one engaged in continuous scientific pursuit of the various branches of exact sciences in relation to medicine. All the functions of the pathologist are not only too numerous but also time consuming.

In order that his work may be successful, he has to devote his undivided attention to the institution on a full time basis. To do his best the pathologist has to be freed from too many cumbersome outside interests, which he is sometimes forced to undertake to eke out his existence.

The hospital will be amply rewarded not only with high scientific standards, which is the pride of an institution, but by being able to offer the best possible care of the patients who come to it for diagnosis and treatment.

410 Fairmount Avenue.

ABSTRACT OF DISCUSSION

DR. WILLIAM CARPENTER MACCARTY, Rochester, Minn.: To live up to Dr. Alter's ideals, a pathologist would of necessity be a superman. He would have to be a tissue pathologist, bacteriologist, serologist, immunologist, protozoologist, chemist, somewhat of a clinician, super laboratory technician, toxicologist, hygienist, medicolegal expert, experimentalist, and in some hospitals a roentgenologist. Above all he would of necessity be an executive of no mean ability. When I first became a pathologist I was expected to do all of these things except roentgenology. I soon realized that no one man could master all these fields. I therefore suggested a division of responsibility, each division being placed in the hands of an expert. In a large institution is the only way the function of pathology can be carried out efficiently. The smaller hospitals for economic reasons will quite naturally have to be satisfied with lesser degrees of general expertness. Realization of this necessity has been responsible for the development of commercial or special independent laboratories, which serve a whole community. In laboratories that serve a greater number of physicians than can a small hospital, the financial returns permit greater division of function among technical experts who are supervised by an executive familiar with the various phases of this great field, which now has so many divisions. In our institution there are many independent subdivisions, each larger than the original department twenty-five years ago, and the members of one division are not and probably could not be trained to do the work of any other division. The directors of each subdivision would not consider themselves capable of assuming responsibility of any of the other subdivisions. I believe the term pathologist will eventually disappear as a designation for a specialist in medicine and will assume a broad significance, such as has the term philosopher. It probably will have no greater specificity and at the same time apply to individuals who deal with all abnormal states or phases of life, even including sociological abnormality. Dr. Alter's paper will serve, I hope, to impress on the general profession the great changes that have occurred in scientific medicine in the last twenty-five years.

DR. NICHOLAS M. ALTER, Jersey City, N. J.: I agree with Dr. MacCarty that the pathologist is almost a superman. It is difficult to define pathology. The best definition is that it is a study of diseases. The study of diseases has progressed and widened enormously, and the pathologist as a full time scientist of the hospital is expected to know a great deal. The reason I brought this question up is that higher standards are wanted for those scientists who are called pathologists and more respect than most hospitals now give. Today hospitals are apt to employ pathologists who have very rudimentary experience. Higher standards will benefit both the pathologist and the hospital.

THE CAUSE OF DEATH IN PNEUMONIA

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My purpose in this study was to investigate the immediate cause of death in pneumonia, both from a clinical and from an anatomic standpoint. The material consists of 200 consecutive cases of pneumonia, which were studied clinically and which finally came to autopsy in the Fourth Medical Service at Bellevue Hospital.

The autopsies were performed by various members of the pathologic staff under the chief pathologist, who has permitted me to utilize the material in this manner. The clinical studies were based on the usual records of the cases under the regular attending physicians and their associates of the division, with additional notes when possible of the immediate manner of death.

During the war as chief of medical service at the Camp Upton Base Hospital, as senior consultant in medicine to the Second Army, A. E. F., 1918-1919, and finally after the armistice attached to the army laboratory at Dijon, France, for this purpose, I made a study of this subject augmented by an analysis of the postmortem records of 5,000 fatal cases of war pneumonia in the American Expeditionary Forces. The summary of this study indicated that most of the patients dying from pneumonia in the American Expeditionary Forces during 1917-1919 did so with a terminal cardiac failure and a final dilatation of the right heart. I felt, however, that the prevalent type of pneumonia occurring in the army during this period was a special form and that conclusions deduced from this material do not fully pertain to the types of pneumonia usual in New York City and its environs. These data, therefore, are not considered in the present study, although observations then made on this enormous material cannot but influence one's point of view to some extent.

In the present series of 200 consecutive fatal cases, no differentiation has been attempted to segregate the various anatomic types of pneumonia, since the histologic process is essentially identical in all. The requirement has been that all should have had as their apparent etiologic factor one of the various forms of pneumococci. Nearly all these cases were typed, either from the blood or sputum ante or post mortem, but since so many forms of pneumococci are now recognized, though sometimes with difficulty, and since the bacterial type furnishes no apparent relationship to the

From the Fourth Medical Service, Bellevue Hospital.
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manner of death or to the pathologic changes studied post mortem, no subclassification has been attempted.

The group comprised 174 males and 26 females. One patient was within the first decade, three were within the second decade, thirty-two were in the third decade, thirty-two were of the fourth decade, thirty-six were of the fifth, fifty-one were of the sixth, thirty-three were of the seventh, eleven were of the eighth, and one was of the ninth decade.

Clinical study of the manner of death from ward observation and from the histories and charts, with particular reference to the type of exitus, indicated the death to be due apparently to cardiac failure in seventy-seven instances. It is significant to note that at autopsy 116 cases showed definite chronic cardiac disease which clearly existed before the onset of the pneumonia. This high percentage may bear some possible relationship to predisposition to pneumonia or may indicate the decreased outlook which the subjects of chronic cardiac disease present against fatal termination in pneumonia. Seventy-three cases showed acute cardiac lesions which developed clearly during the disease and which played a very certain rôle in the termination by death. The heart was mentioned as normal, or entirely ignored among the factors concerned in death in but twenty-nine instances. Fourteen cases showed acute valvular endocarditis.

These data, I believe, substantiate the impression of most experienced clinicians that patients with pre-existing cardiac disease are particularly bad risks in pneumonia and that both clinical and pathologic observation confirms the commonly accepted conclusion that death occurs with greatest frequency with the clinical picture and the pathologic changes of heart failure.

No clinician of experience, however, can be blind to the fact that cardiac failure alone is not the sole factor in death in pneumonia from circulatory failure. Death from circulatory failure is often preceded by days, hours or moments of dilatation and congestion of the capillaries and veins, while the heart action itself is still apparently fairly maintained. There can be no question whatever that vasomotor paralysis of the superficial and deep capillary beds is a most important factor in the picture of circulatory collapse. One hundred and nine instances, inclusive of the seventy-seven cardiac cases cited, showed this type of circulatory failure. Definite and reasonably efficient methods exist for the support and maintenance of cardiac action, but there are all too few efficient means for the treatment of peripheral circulatory collapse. If these symptoms and signs are improved as by the action of solution of pituitary or epinephrine, with a resumption of relatively normal blood pressure and relief of capillary congestion, improvement in the status of the case follows in some instances. No amount of oxygen administration in any form appears either to obviate or to improve these conditions when they appear in failing cases of pneumonia.

It is universally recognized by practitioners that a positive blood culture in any bacterial type of pneumonia is one of the most serious, if not the most grave, prognostic signs that may appear in an early stage of pneumonia. This study fully confirms the general clinical impression that septicemia is in all probability the one most constant serious clinical sign of grave import.

In this series of 200 fatal cases, either positive blood cultures or definite pathologic signs of septicemia found at postmortem were shown in seventy-five cases. Clinical study of the charts confirms this conclusion fully. Thus, fourteen cases showed active acute endocarditis, thirteen cases acute meningitis, twenty cases empyema, and six lung abscess. In many cases a septic type of temperature with profound toxemia even in the absence of confirmatory blood cultures appears to have precisely the same sinister prognostic weight as positive cultures.

I am of the opinion that the degree of sepsis present is the most significant factor in prognosis in the disease and that its presence is the most frequent basic cause of death. It was clinically or bacteriologically diagnosed as present in ninety of the 200 fatal cases. In septic cases, death may occur from terminal cardiac failure, from pulmonary changes or otherwise; the first mentioned manner of death, however, appears to preponderate in this series.

Meningitis has been found to be a frequent immediate cause of death in this group. Whenever it has appeared, it has been an index of sepsis. Its occurrence bears no relationship to the extent or location of the lung invasion, or apparently to the type of pneumococcus present. It was present as the dominant cause of death in thirteen instances in this series. It had been correctly diagnosed ante mortem in all cases. It has been the custom of many clinicians, myself among them, occasionally to recognize a clinical picture known as meningismus, a condition with sterile spinal fluid but with the clinical indications of cortical irritation. As a result of these studies I am convinced that there is no such condition as meningismus in pneumonia but that all instances so diagnosed are in reality cases of meningitis or of encephalitis. I believe however that in certain mild cases of these, recovery may occasionally, though rarely, occur. This statement will be disputed by some excellent and experienced authorities beyond doubt.

The degree in which anoxemia plays a dominant rôle in the immediate cause of death in pneumonia is exceedingly difficult to ascertain with any satisfactory degree of certainty. Accurate studies of this nature would as yet imply methods of such character as more or less seriously to hazard the welfare of the human patient. The mere chemical study of the blood furnishes very insufficient data for this purpose, and one probably can do little more in the ordinary clinical case than to study and attempt to estimate the value of oxygen administration to apparently moribund patients, just as one attempts to evaluate similar clinical methods for the relief of circulatory failure.

So far as my observations go, the extent of lung involvement is of but minor value as a prognostic factor in death in pneumonia. Thus, of the present group, fifty cases showed involvement of but a single lobe, in forty-two two lobes were invaded, in nineteen three, and in eighteen four or five lobes were cited as involved. In seventy-one instances the extent of lung involvement was not adequately defined in the histories or protocols.

Obviously the adequate use of oxygen by the newer methods of administration should afford strikingly valuable evidence as to the importance of anoxemia in the determination of death in pneumonia. Naturally, at the present time, a very wide difference of opinion exists in regard to this method of therapeusis; the matter is still in active dispute. That oxygen tremendously increases comfort in many cases and that it often prolongs life, seem to be facts beyond dispute, but in my observation it has little if any permanent effect in septic cases or in those in which grave circulatory defects have developed. I do not feel that it manifestly modifies prognosis materially, in cases showing grave

pathologic changes, such for example as in massive collapse, atelectasis or embolism.

Of the cases in which pulmonary changes seemed to play the important rôle in the cause of death, I must cite twenty cases of empyema, in which lung compression had been considerable, but in all of which a basic septicemia was present; atelectasis due to plugging of a bronchus with tenacious exudate was present in nine instances, and massive collapse in four. In none of these last mentioned lesions had the precise nature of the pathologic condition been recognized clinically, and subsequent observation has convinced me that these lesions are much more frequent and very much more important than I, at least, have previously recognized. In the four instances of massive collapse this lesion was in all probability the immediate cause of death, and in at least some of the nine cases of atelectasis it too had been an important immediate lethal factor. Pulmonary embolism, which I previously esteemed to be a not infrequent immediate cause of death in pneumonia, occurred but once and the lesion in this case was very small and probably relatively unimportant. I suspect that massive collapse and atelectasis from various causes have generally been mistaken for pulmonary embolism. Emboli other than in the lung occurred in but two instances, in neither of which did it seriously contribute to the fatal outcome. Pulmonary gangrene was a prominent lethal factor in two instances.

Most textbooks stress the importance of tuberculosis in connection with death in pneumonia. Chronic healed pulmonary tuberculous lesions were found in but eighteen cases of the series. In none of these did they play a rôle in the cause of death. In two cases, however, there had developed an activation of an old lymphatic tuberculosis with generalized tuberculosis and death as a result. It is very probable that most physicians have overestimated the rôle of tuberculosis as a fatal factor in the termination of pneumonia.

Many physicians, including myself, have much emphasized the rôle which alcoholism plays in the fatalities from pneumonia. In this series but five instances of this nature appeared. It is then quite possible that we have been overestimating this factor in pneumonia fatalities, but I cannot refrain from stating that I nonetheless feel that chronic alcoholism, with its attendant exposure and other concurrent factors, at least looms large as an important factor in susceptibility to the disease. Ten instances of this probable relationship, including the five cases already cited, seem to bear out this assumption.

Wonder has often been expressed because so few cases of pneumonia terminate from serious renal defects, for renal irritation and congestion are usually a prominent sign at onset. Only three instances in which active nephritis was present were observed in this series. In none of them had it assumed clinical importance, nor was it cited as a contributory factor in the cause of death.

Very numerous other and exceedingly interesting facts have discovered themselves in this brief study. The limitation of this paper, however, permits discussion of only the most important and striking observations. Grounds for many studies both in the clinic and in the deadhouse have, however, been suggested, and though the subject may seem to some to be threadbare and reduced to mere osteology by the overwhelming literature concerning the bacteriology and serology of pneumonia that has appeared in recent years, it is apparent to the student of clinical medicine that much time may still be profitably spent in the study of the clinical features and pathology of pneumonia.

CONCLUSIONS

I feel that the facts cited justify the following conclusions:

The most serious basic factor in the cause of death in pneumonia is sepsis.

Patients with pneumonia most frequently die immediately from circulatory failure. In this term must be included both essential cardiac failure and peripheral vasomotor paralysis.

Anoxemia is not a frequent immediate cause of death in pneumonia.

Atelectasis and massive collapse are probably more frequent as terminal factors than is generally supposed.

Embolism and thrombosis are probably rare as terminal causes in pneumonia.

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ABSTRACT OF DISCUSSION

DR. J. H. MEANS, Boston: Some eighteen years ago I had the privilege of working with Dr. L. H. Newburgh on this problem. That work, I think, is largely out of date, but I will mention it briefly. Dr. Newburgh tried, both in the clinic and experimentally, to answer this very question Dr. Brooks has been attacking. Do the patients die of a vasomotor collapse or is the vasomotor center exhausted? The methods used seemed to give a negative answer to that; the vasomotor center carried on effectively. An attempt was made to answer in experiment whether death is due primarily to myocardial failure. The study was carried out in dogs, the Friedländer bacillus being used. I have to admit that it is quite remote from human pneumococcic pneumonia. These experiments seemed to show that the heart muscle carried on fairly well and that the blood was poisonous to it. Then the respiratory center was studied in dogs with Friedländer pneumonia, and some evidence seemed to indicate failure. This again was far removed from human lobar pneumonia. Since then other things have come up for consideration. At one time I thought that acidosis played an important rôle in pneumonia—carbon dioxide acidosis. I doubt this now. I don't believe it plays any rôle at all. I don't believe that the rôle of anoxemia in death from pneumonia is known. I do think oxygen therapy should be used. If I had pneumonia and was cyanotic, I should want oxygen given. It is impossible to determine with any degree of statistical accuracy whether a given method of treatment reduces mortality or not. I use oxygen therapy for any patient with pneumonia who is unduly cyanotic or shows undue respiratory stress. Likewise, when the circulatory symptoms loom big, oxygen therapy should be used and used reasonably early before the patient is actually moribund. These patients have a chloride deficiency, and my colleagues Dr. A. V. Bock and John Talbott have some evidence to show that it is desirable to give the patient with pneumonia a large salt intake to offset the chloride loss, because deprivation of chlorides leads to untoward symptoms. Intoxication, sepsis and infection play an important rôle.

DR. L. J. MOORMAN, Oklahoma City: Present knowledge of the ultimate phenomena of life and death is inadequate. No doubt every thoughtful clinician will acquiesce in the belief of Dr. Brooks that, in the great majority of cases, the ultimate cause of death in pneumonia is circulatory failure. Those who have entertained this belief welcome the corroborative evidence revealed by his investigations. However, for the benefit of those who may be content with the present understanding of the cause of death in pneumonia, attention is called to certain principles expressed by Aretaeus seventeen centuries ago. In the translation by Francis Adams is the following introduction to the chapter on pneumonia: "Animals live by two principal things—food and breath. Of these by far the more important is respiration. In the midst of the lungs is seated a hot organ, the heart, which is the organ of

life and respiration. If, therefore, the heart suffers primarily, death is not far off." With a liberal interpretation of this statement, it must be admitted that Aretaeus, seventeen hundred years ago, was observing and recording the same phenomenon observed and recorded by Dr. Brooks. It has been said that life has but two legs on which to stand, the heart and the lungs. Bichat taught that death may have its origin in the heart, in the lungs or in the head. Since the nerve centers hold the secret of life and death, Bichat's teachings must be accepted. However, it should not be forgotten that the vital centers cease to function the moment circulation becomes inadequate. Though death may seem to be due to respiratory failure or to interrupted function of the vital centers, in the last analysis it is, in all probability, circulatory in origin. Limited knowledge with reference to the cause of death constitutes a serious indictment of the medical profession and suggests a fascinating field for future investigation. May I suggest that well organized hospitals consider the advisability of team work in the study of the cause of death; the coordinated efforts of the experienced clinician, the skilled physiologist, the biochemist and the pathologist should ultimately lead to definite advances in knowledge regarding this difficult problem.

DR. MAXWELL FINLAND, Boston: Dr. Brooks has rightly emphasized the importance of bacteremia and the consequent focal infections as the most serious factor in the cause of death from pneumonia. Bacteremia may be considered a manifestation of the failure of the immunologic defense. Our experience with serum treatment at the Boston City Hospital has led us to feel that the administration of type-specific antibody helps to overcome this difficulty. This is evidenced by the rapid and permanent clearing of the bacteremia or by preventing its appearance, and also by the prevention of the spread of the pulmonary lesion. To attain such an effect the antibody must be type specific for the invading organism, and it must be given in adequate amounts and early enough in the disease. When the infection has progressed to a stage at which the fixed and circulating phagocytes have been sufficiently injured, or when purulent foci have become established, we feel that such antibody is of little avail. In considering circulatory failure, which Dr. Brooks has noted as the important immediate cause of death, one must take into account the degenerative changes related to age. The well established fact that the death rate from pneumonia increases steadily with advancing age depends largely on this factor. Among our type I patients, 56 per cent were under 40 years of age and only 23 per cent were over 50. In spite of this well known predominance of type I pneumonia in the younger age groups, only 28 per cent of patients with this type coming to autopsy were under 40, and 58 per cent were over 50. Among the latter, chronic cardiovascular lesions, either gross or microscopic, were the rule. Among nineteen patients under 50 years of age, however, the only cardiac abnormalities noted were two instances of right-sided dilatation, one case showing acute vegetations grafted on a healed rheumatic endocarditis, and one case of fibrinous pericarditis. Our incidence of endocarditis is considerably lower than occurred in the series of Dr. Brooks. I am interested in the frequency of so-called acute cardiac lesions in the cases of Dr. Brooks. It is not clear to me what conditions are included among such lesions. In the cases of pneumococcic pneumonia which Dr. Sutliff and I studied, instances of acute necrosis of the myocardium, either infectious or toxic, were not encountered. Dr. Parker, director of the Mallory Institute of Pathology, who examines microscopically the sections from our cases, believes that such changes are extremely rare in pneumococcic pneumonia. He has encountered such necrosis, however, in cases of hemolytic streptococcus sepsis. Since most of the cases in the army were in young adults, I should like to ask Dr. Brooks whether the high incidence of cardiac dilatation noted in the camps might not have been related to the frequency of hemolytic streptococcus invasions complicating the pneumonias at that time, particularly those related to epidemics of influenza and measles. We have not encountered any instance of meningismus in which lumbar puncture revealed normal spinal fluid and in which evidence of an inflammatory lesion of the brain or meninges was discovered at autopsy. I should like to ask whether Dr. Brooks' opinion in regard to meningismus is based on such observations.

DR. ROBERT G. TORREY, Philadelphia: Dr. Brooks called attention to the importance of circulatory function in pneumonias and minimized the toxic effect of pneumococcic infections. There is no chance for denial of the importance of the toxic factor with profound and prolonged sepsis, but most of our cases do not show that picture. Most of these patients die of circulatory failure. Dr. Brooks dwelt less on the failure of the pulmonary than of the peripheral circulation, but I believe observation will indicate that the sudden change evident in the patient with the onset of pneumonia and the stress is due to failure in the pulmonary circulation. It is a sudden failure which causes the distress characteristic of pneumonia, and its prolongation causes a vascular strain, which is reflected in peripheral failure. All physicians are interested in the treatment of pneumonia, and that consists in combating these complications. Pulmonary congestion, with its respiratory difficulties, and pulmonary edema, or wet lung, have to be met by heroic measures. It seems reasonable not to wait to meet this circulatory strain when it occurs but to forestall it if possible. In the past two years I have treated patients at the Philadelphia General Hospital and at the Woman's College Hospital with measures aimed at this end as a routine, and I have been more than satisfied with the apparent results. That is, in cases showing respiratory distress seen early, very drastic dehydration is attempted by eliminating fluid intake to 24 ounces in twenty-four hours, limited to orange juice or milk with no added water, and no other food. The patients complain much less than would be imagined, and the relief seems to be gratifying. We combat coughing and distress with sedatives, preferably powder of ipecac and opium, in small doses at frequent intervals in the beginning. This probably also encourages sweating, thus aiding dehydration. It seems more reasonable to reduce the work of the heart and the circulation early than to try to combat the failure after serious damage has been done. Simple and very drastic and severe dehydration seems to have a reasonable effect in reducing what used to be called toxemia but which is now believed in many cases to be pulmonary circulatory distress.

DR. A. L. BARACH, New York: One has to view lobar pneumonia not only as a disease characterized by pneumococcic toxemia or by terminal circulatory failure but also by a variable disturbance in the oxygen absorbing function of the lung. In a series of 285 cases at the Presbyterian Hospital in the past eight years I have observed twelve cases in which oxygen treatment was withdrawn before the disease process in the lungs had cleared. The resultant collapse was evidence of the sustaining effect of oxygen, as was also the fact that most of them returned to their former state when oxygen was again provided. Before it was known that anoxemia was a factor in the mortality of pneumonia, two patients were taken out of an oxygen room prematurely. The circulatory and respiratory failures were so severe as ultimately to cause death. The second function of the lungs, the elimination of carbon dioxide, presents no difficulty to the pneumonia patient. However, in those cases in which marked pulmonary involvement is present, the inhalation of 50 per cent oxygen frequently sustains life until the patient is able to develop immunologic resistance to his disease. When circulatory failure is spoken of, one ought to bear in mind that oxygen want is itself a noted cause of circulatory failure. Myocarditis has been produced by exposure to a lowered content of oxygen in the inspired air in animals. The degree of arterial anoxia required to accomplish this may not infrequently occur in the pneumonia patient. Granted that sepsis is a frequent cause of death, one must also grant, as Dr. Finland pointed out, that the death of many pneumonia patients is associated with the maximal lung involvement. I think it is fair to state, therefore, that one must bear in mind the function of the damaged lung in the treatment of pneumonia as well as the toxemia caused by the pneumococcus organism.

DR. HARLOW BROOKS, New York: I worked at this subject during the war and have been working at it ever since. Every alternate patient who has come to my service during these years has received some specific method of treatment.

I wish I were as enthusiastic about the use of serum as I was ten years ago. We have a corps of workers especially trained to conduct this work with my full cooperation. Their faith is beginning to waiver as they see more cases. So I have said nothing about specific serum. My object is to find out how they died; then perhaps I may find out why they died, and then some other generation may find out how to keep them from dying. That I feel no one is prepared to speak on with much authority as yet. The war streptococcus cases are probably not similar to those on which these data of today are based. It was the type of the exudate and the embarrassment of the pulmonary circulation, which Dr. Torrey mentioned, which would probably distinguish this type of pneumonia, the A. E. F. type, from that with which we are dealing at present. The question of peripheral circulatory failure is an exceedingly interesting problem. We have been working on the chemical and bacteriologic sides of this subject also but I, dating back to my original training, have taken the pathologic side of the question. Until we know how they die, I do not think we shall be able to change the mortality rate.

NEUROLOGIC MANIFESTATIONS OF HYPERINSULINISM AND OTHER HYPOGLYCEMIC STATES

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The neurologist so frequently is confronted with diagnostic problems involving bizarre nervous symptoms that he should acquaint himself with syndromes which may have as a predominating symptom some nervous manifestation, although the underlying disease may be outside his special field. Hyperinsulinism and hypoglycemia are conditions of this type, and, although not primarily of neurologic importance, the presenting symptoms may be of a distinctly nervous character.

Symptoms from both overactivity and underactivity of the endocrine glands generally have been recognized. Thus both exophthalmic goiter and myxedema have been attributed to the thyroid gland for many years. For some unknown reason, however, the recognition of symptoms resulting from the overactivity of certain glands has lagged behind the recognition of the symptoms of underactivity. Diabetes, parathyroid tetany and hyposuprarenalism (Addison's disease) were described long before hyperinsulinism, hyperparathyroidism and hypersuprarenalism.

We are limiting this paper to conditions that are the antithesis of diabetes, in which symptoms are produced by an insufficiency of sugar in contrast to an excess. Further, we are going to focus our attention more on symptoms than on pathologic conditions or on treatment, and special attention is to be called to the preponderance of neurologic symptoms in these conditions. No effort is made to review in detail the rapidly accumulating literature on the subject; such a review may be obtained from any thorough article.[1]

Many efforts have been made to classify the possible causes of hypoglycemia, and a very good classification is the one given by Wauchope,[1] as follows:

1. Excess of insulin. This may be the result of therapeutic injections of insulin, of tumors and hyperplasia of the pancreas, or of functional hyperinsulinism (idiopathic hypoglycemia).

2. Lack of opposing secretions. This condition may result from disease of the suprarenal glands, from tumors of the anterior or posterior lobe of the pituitary body, or from myxedema.

3. Lack of glycogen. This lack may result from destruction of reservoirs, from disease of the liver or wasting of muscles, from abnormal secretion of sugar, from renal diabetes, from lactation, from active depletion of stores, such as occurs in muscular exercise, and from failure to replenish stores as in starvation.

4. Interference with regulating center. This may result from another nervous disease which affects the pons, or from overaction of the vagus nerves.

These causes usually are complex, and they must be so because the mechanism involved in the metabolism of carbohydrate is so complicated. Many factors are involved in the metabolism of carbohydrates; among others, the amount of carbohydr ingested and the amount absorbed, the production of glycogen and its deposition in liver, muscles and other tissues, and glycogenolysis and utilization of dextrose. Any condition that interferes with any of these steps will itself produce symptoms which further add complexity to an attempted classification of the causes of hypoglycemia. Thus many investigators who have attempted to classify these etiologic factors have as one heading "endocrine disturbances," beneath which is listed practically every endocrine gland in the body. Perhaps this is justified; perhaps every endocrine gland does affect carbohydrate metabolism. However, it is difficult to see how this clarifies the situation. Diagnosis is the most important part of the problem of hypoglycemia. Once the diagnosis has been made, the various steps in carbohydrate metabolism can then be reviewed and an attempt made to locate the precise etiologic factor responsible. Just how difficult this is can be appreciated only by one who has tried to do it.

Strangely enough, the symptoms of hypoglycemia have been known only since the discovery of insulin in 1921.[2] It was not until 1924 that Harris[3] called attention to the possibility that hypoglycemia might develop among certain patients from an oversupply of the patient's own insulin, and it was not until 1927 that such a case was reported;[4] namely, that of a physician who suffered and finally died from spontaneous hypoglycemia due to carcinoma of the island cells of the pancreas. Since then, numerous other cases of hypoglycemia from tumors of the island cells have been reported, and many patients have been cured by surgical removal of the adenoma. Another group of cases of hypoglycemia has been reported in which the condition resulted from primary disease of the liver.[5]

From the Division of Medicine and the Section on Neurology, the Mayo Clinic.

Read before the Section on Nervous and Mental Diseases at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 13, 1934.

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4. Wilder, R. M.; Allan, F. N.; Power, M. H., and Robertson, H. E.: Carcinoma of the Islands of the Pancreas: Hyperinsulinism and Hypoglycemia, J. A. M. A. **89**: 348-355 (July 30) 1927.

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The pituitary gland is suspected of being of etiologic importance in other cases of hypoglycemia, and, while there is experimental evidence to bear out this relationship, there have been no proved clinical cases, although Josef Wilder [6] suggested this diagnosis in two cases.

Cases that are clear-cut examples of uncomplicated hypoglycemia are those in which symptoms definitely are the result of hypoglycemia and in which removal of a tumor of the island cells of the pancreas causes disappearance of all symptoms. The patients in such cases may be said to suffer from hyperinsulinism, a term often loosely applied to a variety of vague symptoms among patients whose pancreas never is examined. They complain of the same symptoms as does the diabetic patient who has received an excessive amount of insulin, and every physician is familiar with such symptoms. These patients are perfectly normal after the ingestion of carbohydrate food. Such a history, together with a low reading for blood sugar, is all that is necessary for the diagnosis of spontaneous hypoglycemia. The advisability of surgical exploration to establish the presence or absence of adenoma of the island cells of the pancreas will be considered later.

There is no doubt that hundreds of persons are suffering from undiagnosed spontaneous hypoglycemia. This paper is being presented for the consideration of neurologists and psychiatrists because we believe that they have the best opportunity of making this diagnosis, since by the very nature of the symptoms these patients present what appears to be a neurologic problem; this was pointed out by Harris,[1] by Wolf and his associates [7] and by others.

In preparation for this paper we reviewed all cases of spontaneous hypoglycemia that had been reported, to see how many patients presented neurologic symptoms. The answer was quickly obtained: they all had neurologic symptoms of one type or another. The striking feature was the fewness of symptoms that were not neurologic,[8] evident in Tedstrom's report, as follows: Weakness or prostration occurred in thirty-seven cases, and its allied condition of fatigue in ten cases; that is, forty-seven cases, the two symptoms taken together. Stupor occurred in seven cases and coma in thirty-nine; that is, forty-six cases, the two symptoms taken together. Muscular twitching occurred in eight cases and convulsions in twenty-six cases; that is, thirty-four cases, the two symptoms taken together. Loss of memory occurred in twenty cases, sweating in nineteen and change in general behavior in eighteen. Disturbance of speech was encountered in eighteen cases, as follows: Speech was unintelligible in eight cases; motor aphasia was present in five cases, and the speech was slow in three cases, monotonous in one case and slurring in one case. Nervousness was a characteristic in fifteen cases. Restlessness occurred in eight cases, and its allied condition, mania, in seven cases; that is, fifteen cases, the two symptoms taken together. Fourteen patients were mentally confused, and the same number had epileptiform seizures. In twelve cases hunger was excessive. Ocular symptoms were present in twelve cases, as follows: diplopia in five cases, dimness of vision in three cases, dilated pupils in two cases, blurred vision in one case and unequal and miotic pupils in one case. Ten patients were troubled with vertigo, and an equal number with dulness and listlessness. Nausea was present in three cases and vomiting in seven; that is, ten cases, the two symptoms taken together. Headache was present in nine cases and drowsiness in nine. Each of the following symptoms was found in a respective group of eight cases: fainting, tremors, epigastric pain and a positive Babinski sign. Vague paresthesia was encountered in six cases. Loss of sphincteric control, irritationality and emotional instability were characteristic, each in a respective group of five cases. Four patients foamed at the mouth, and four were pallid. Three patients had fear of death.

Attacks of unconsciousness and even convulsive seizures often are prominent symptoms and, not uncommonly, a diagnosis of epilepsy is made in these cases. This naturally calls attention to the need for considering hypoglycemia as a possible etiologic factor in every case in which the patient presents himself with a history of having had convulsions. Because of the behavior disturbance and other associated symptoms a diagnosis of acute alcoholism occasionally is made. One of our patients carried a slip of paper on which was written "I am not drunk, I am sick. Make me drink orange juice if you can; if you can't, call Dr. ———." We have seen cases in which a diagnosis of tumor of the brain, and even of insanity, had been made when patients were suffering from hypoglycemia, and in which, following administration of carbohydrates, the patient made a miraculous although temporary recovery. Attention also is called to the frequent presence of a positive Babinski sign, which disappears when the blood sugar is raised to normal levels. It should be mentioned that the severity of symptoms varies with different individuals and with different levels of blood sugar. Some patients have severe symptoms when the concentration of sugar is 60 mg. per hundred cubic centimeters of blood; others have few symptoms when the blood sugar is 40 mg. One of us (Rynearson) during the course of an experiment was found to give a reading for sugar of 30 mg. per hunderd cubic centimeters without appreciable symptoms.

It is an interesting commentary that, frequently, in cases in which spontaneous hypoglycemic attacks occurred, the patient or some member of his family had discovered that a relationship existed between the attacks and the ingestion of food. The following case exemplifies this:

CASE 1.—A laborer, aged 45, had enjoyed good health until four years prior to his admission to the clinic. At that time he had begun to have symptoms resembling those of drunkenness. These had occurred between meals, had been much more likely to occur if he had worked hard, and had been relieved by taking food. On one occasion he had had a characteristic epileptiform seizure, followed by unconsciousness, which had lasted sixteen hours. When he awoke, he had been mentally confused until he had drunk some milk, when he rapidly had become normal. About this time he and his friends had realized the value of food in relieving these symptoms, so that on another occasion, when he had been unconscious for twenty-six hours, a friend had revived him by forcing him to drink milk. He had complained of a severe headache, in conjunction with these symptoms, which had persisted in varying forms during the entire four years.

The clinical diagnosis of spontaneous hypoglycemia was confirmed by a reading for blood sugar of 30 mg. per hundred cubic centimeters. At operation, a tumor of the island cells of

6. Wilder, Josef: Ein neues hypophysäres Krankheitsbild: Die hypophysäre Spontanhypoglykämie, Deutsche Ztschr. f. Nervenh. **112**: 192-250 (March) 1930.

7. Wolf, A.; Hare, C. C., and Riggs, H. W.: Neurological Manifestations in Two Patients with Spontaneous Hypoglycemia with Necropsy Report of Case of Pancreatic Island Adenomata, Bull. Neurol. Inst. New York **3**: 232-251 (June) 1933.

8. Tedstrom, M. K.: Hypoglycemia and Hyperinsulinism, Ann. Int. Med. **7**: 1013-1025 (Feb.) 1934.

the pancreas was discovered, which was diagnosed carcinoma. Immediately following the operation the level of sugar in the blood returned to normal and hypoglycemia never occurred again. The patient has been in excellent health since the operation and has not had symptoms of any sort.

In this history there are several important features: the patient's symptoms were present only when he was hungry, they often were produced by exercise, they were essentially of neurologic character, they were relieved by the ingestion of carbohydrate, and they disappeared entirely following surgical removal of an adenoma of the island cells of the pancreas.

Medical treatment of hyperinsulinism has uniformly been unsuccessful. It is true that certain patients with symptoms of hypoglycemia of unknown etiology may obtain relief from such medical measures as frequent feedings, but in these cases a diagnosis of hyperinsulinism should not be made; a diagnosis of hyperinsulinism should be reserved for cases proved at operation or at necropsy.

Regarding the character of the tumor, Bensley [9] recently has written: "I wish very much that I could say something which would stop the clinical people from calling these tumors associated with hypoglycemia 'beta cell tumors.' The one thing that is conspicuous in all that I have examined so far is that they are actually neoplastic cells with some resemblances to island cells, probably producing insulin or some related substance." Certainly this opinion has strong clinical support. It is discouraging to operate on a patient who has had hyperinsulinism for years and find that, because of delay in diagnosis or in surgical intervention, the adenoma has become inoperable as a result of extensive metastasis. So many carcinomas give no warning signs of their presence; yet here is one type that shrieks for attention. It would seem advisable to subject all patients with this syndrome to abdominal exploration, since there is no method at present of diagnosing a tumor preoperatively. The exploration itself is attended with little risk; no deaths have been reported as a result of it. If a tumor of the island cells of the pancreas is not found, treatment must, in view of present inadequate knowledge, remain palliative.

The mechanism involved in the production, by hypoglycemia, of neurologic and psychic symptoms is not definitely known. Olmsted and Logan [10] expressed the belief that insulin convulsions are caused by the action of insulin on the bulbar centers. They found that decapitated cats do not have convulsions, despite a low concentration of sugar in the blood, whereas convulsions are marked in decerebrate cats. They also presented evidence to support the hypothesis of the antagonism of solution of pituitary to insulin. Rudy [11] expressed the opinion that convulsions are the result of hypoglycemia itself, whereas Drabkin and Ravdin [12] felt that convulsions are related to water balance, since they had observed that water-starved dogs did not have convulsions despite pronounced hypoglycemia. Although the exact mechanism of the production of hypoglycemia is still unknown, it is definitely established that all tissues require sugar for normal function.

Patients suffering from convulsions or from temporary psychic disturbances should be investigated as to the possible presence of spontaneous hypoglycemia. Studies of the blood sugar in clear-cut cases of epilepsy have indicated relatively normal levels,[13] although immediately following a seizure the amount of sugar in the blood may be low, owing to the tremendous exertion.

Among patients suffering from personality disorders, Henry and Mangam [14] found relatively normal sugar tolerance curves. The presence of marked hypoglycemia, therefore, should be very suggestive, and further investigation should be carried out to determine its importance as an etiologic factor in the production of such neurologic or psychic symptoms.

SUMMARY AND CONCLUSIONS

This paper is presented to emphasize the universal occurrence of neurologic and psychic symptoms in severe hypoglycemia. It is hoped that through the cooperation of neurologists and psychiatrists many hitherto undiagnosed cases of hypoglycemia may be discovered. In the light of present inadequate knowledge, medical treatment is unsatisfactory, and it is only by early surgical exploration in these cases of hypoglycemia that adenomas of the island cells of the pancreas may be found and successfully removed. It is to be hoped that the time is not far off when it will be possible accurately to separate the various types of hypoglycemia and to treat each type better.

ABSTRACT OF DISCUSSION

DR. I. S. WECHSLER, New York: The paper of Drs. Rynearson and Moersch calls attention to a problem that is occasionally confusing. I don't think it is quite as common as one might get the impression, although I have seen at least half a dozen different reactions to hypoglycemia and hyperinsulinism. I am glad the authors make proper distinction between the two conditions, as it is important clinically and pathologically to distinguish between them. I have seen a case of hemiplegia in which all the signs disappeared promptly with the administration of dextrose. This patient had received an excessive dose of insulin. The occurrence of a Babinski sign in hyperinsulinism without hemiplegia is rather well known. I saw a patient who had convulsions and died of adenoma of the pancreas. The patient used to slump, have convulsions, thrash about, become unconscious for a long time, and spontaneously come out of the stupor. I have also seen one case of epilepsy following hypoglycemia. Recently I have seen patients with all sorts of psychiatric manifestations, abnormal involuntary movements such as chorea and dystonia, and bizarre hysteroid manifestations. There is no doubt that many so-called psychoneurotic symptoms occur in the course of hyperinsulinism and hypoglycemia. It is well therefore to make blood sugar determinations in all obscure cases and treat them if necessary. As to subjecting every patient to an operation, that is not so simple. I will take the authors' word for it that the operation is not serious. To me it would rather seem a heroic thing to do; but there may be isolated instances in which one could justifiably do an exploratory laparotomy.

DR. GEORGE W. HALL, Chicago: I have not had much experience with convulsions in these cases. However, I have seen a few cases in which definite neurologic symptoms have appeared. It is interesting to note how few marathon racers have had difficulty after the race. One important point that

9. Bensley, R. R.: Personal communication to the author.
10. Olmsted, J. M. D., and Logan, H. D.: The Effect of Insulin on the Central Nervous System and Its Relation to the Pituitary Body, Am. J. Physiol. **66**: 437-444 (Oct.) 1923.
11. Rudy, Abraham: The Relation of Blood Sugar to the Symptoms of the Insulin Reaction, with a Discussion of the Mechanism of Hypoglycemia, M. J. & Rec. **137**: 463-466 (June 7) 1933.
12. Drabkin, D. L., and Ravdin, I. S.: The Mechanism of Convulsions in Insulin Hypoglycemia, J. Biol. Chem. **87**: iii-iv (June) 1930.
13. Lennox, W. G., and Cobb, S.: Epilepsy, from Standpoint of Physiology and Treatment, Medicine **7**: 105-290 (May) 1928.
14. Henry, G. W., and Mangam, Elizabeth: Blood in Personality Disorders: Biochemical Studies, Arch. Neurol. & Psychiat. **13**: 743-749 (June) 1925.

the authors brought out is that hyperinsulinism may be mistaken for drunkenness. The patient may become neglectful of his work and stagger about as though he were drunk. He feels weak before eating his breakfast and staggers around a great deal. After breakfast he goes along fairly well until lunch time, when he notices that he is weak again. One may be inclined to think he is drinking, but as has been reported in some cases it has been found that the patient does not use liquor in any form. Tests of the blood sugar show that it is much below normal. The symptoms in these cases are necessarily individual. Some will respond in a very different way from others, as the authors have noted.

DR. HARLOW BROOKS, New York: I see a good many minor manifestations of these symptoms among women who are dieting to reduce weight and who cut down their sugar, starch and carbohydrate intake in general. The first case that I saw was one in which a young woman had chosen to reduce her weight and at the same time carry on an active athletic life. The result was a blood sugar of 10, which appeared every morning at 2 o'clock. These conditions are quite frequent, and I am sure that the authors would feel as I do that it would not be wise to do an exploratory laparotomy until the diet had been carefully considered. The low sugar diet, in association with exercise, will frequently cause the whole picture described by the authors. The first case that I saw was under the care of a famous psychiatrist and had been diagnosed as a case of hysteria. It was a case of starvation diet.

DR. TOM B. THROCKMORTON, Des Moines, Iowa: My contact with this rather new entity was thrust on me unexpectedly last summer when a young woman was referred to me from the northern part of the state, suffering from narcolepsy. In association with the narcolepsy a psychasthenic condition had developed in which fear played the predominant rôle. The maternal instinct of the patient was such that she had a great fear something would happen to her baby during one of these attacks of involuntary sleepiness. The general physical and neurologic examination failed to reveal anything, and I so wrote the referring physician. Fortunately, a coincidence happened. In the mail of that day came reprints from Dr. Seale Harris on this subject of narcolepsy associated with hyperinsulinism and the hypoglycemic state. After reading them I immediately wrote the physician that perhaps it might be well if a chemical examination of the blood be made, particularly in regard to the lowering of the sugar content. This was done and he wrote me that a very low blood sugar was found. Following my suggestion that the patient be placed on a high carbohydrate intake, he later stated that she had practically been relieved of her attacks of narcolepsy and that the psychasthenic state of fear had been largely removed.

DR. EDWARD H. RYNEARSON, Rochester, Minn.: Reference has been made to the occurrence of low values for sugar in the blood of marathon runners. In a study of those who finished the 26 mile marathon race in Boston, it was found that there was great variation in the values for blood sugar, depending to a great extent on the runner's physical condition; those who lost usually had low values for blood sugar. Unquestionably, the blood sugar was affected by the amount of carbohydrate consumed during the race. Dr. Brooks referred to a patient whose symptoms improved following her return to a normal dietary regimen. Certainly, in such a case operation should not be performed. However, this case illustrates a point that we have tried to make; namely, the importance of distinguishing the mild and usually vague symptoms of hypoglycemia from the severe symptoms resulting from the marked lowering of the blood sugar resulting from possible hyperinsulinism. We do not advise surgical exploration of the abdomen of a nervous girl the fasting value of whose blood sugar is 60 mg. per hundred cubic centimeters, but we do advise an exploratory operation for a patient the fasting value of whose blood sugar is 20 mg. per hundred cubic centimeters and who is likely to become unconscious if he does not partake largely of foods high in carbohydrate every three hours, both day and night. This has been referred to as a rare condition. Although, unquestionably, it is not of frequent occurrence, I am of the opinion that the condition in many cases is not diagnosed.

THE KRUKENBERG TUMOR

REPORT OF A CASE WITH RECTAL INVOLVEMENT, PRODUCING STRICTURE

F. G. RUNYEON, M.D.
READING, PA.

In 1896 Friedrich Krukenberg described a tumor of the ovary which he called fibrosarcoma mucocellulare carcinomatodes. He considered this tumor to be a fibrosarcoma containing large epithelioid cells enclosing mucin, which induced him to add the name mucocellulare carcinomatodes.

Krukenberg maintained that the tumor was primary in the ovary, a view that has been much discussed and opposed. At the present time most observers consider it to be secondary to carcinoma in some portion of the gastro-intestinal tract.

In 1918 Major [1] in a classic paper collected fifty-five cases from the literature and discussed in a complete manner the opinions expressed by various authors as to the conflicting views concerning its origin, mode of transmission and pathologic appearance.

In 1929 Fallas [2] collected twenty-three more cases, and Enzer [3] collected six cases and reported one in 1930.

TABLE 1.—*Record of Cases Studied*

Reference	Contribution	Cases	Year
Major [1]	Collected	55	1918
Pribram, E. E.: Arch. f. Gynäk. **116**: 343 1921	Reported	1	1921
Fallas [2]	Collected	23	1929
Enzer [3]	Collected	6	1930
Enzer [3]	Reported	1	1930
Tyner, J. D.: Clifton M. Bull. **16**: 93, 1930	Reported	1	1930
Babcock, W. W.: S. Clin. North America **10**: 271, 1930	Reported	1	1930
Stephens, H. W.: Ann. Surg. **96**: 1078, 1932	Reported	2	1932
Runyeon	Reported	1	1934

	Cases
Presenting only ovarian involvement	23
Presenting involvement of organs in addition to the ovary	68
Total number of cases studied	91

These and the other cases reviewed in this article are shown in table 1. Of the twenty-three cases in which only ovarian involvement was reported, only two presented conclusive evidence by autopsy and microscopic study that other organs were not involved.

In the study of Krukenberg tumor there are two pathologic questions that attract attention: First, is this tumor primary in the ovary or is it secondary to some gastro-intestinal carcinoma? Second, how can one explain the combination of malignant connective tissue and epithelial areas?

Fallas [2] says that the primary growth is usually in the stomach but sometimes in the small intestine, the gallbladder and the breast. He says that it is considered primary carcinoma and not sarcoma.

From the Proctologic Department of the Reading Hospital.
Read before the Section on Gastro-Enterology and Proctology at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 15, 1934.
I am indebted to Dr. Frederick Light and Dr. Erwin D. Funk of the Pathological Department of the Reading Hospital for their cooperation in the postmortem reports and the preparation of slides, to Dr. J. C. Bloodgood of Baltimore and Dr. J. I. Fanz of Philadelphia for verification of the pathologic diagnoses and to Dr. Horace Long for his help in the collection of data and reports of previously collected cases.

1. Major, R. H.: A Study of the Krukenberg Tumor, Surg., Gynec. & Obst. **27**: 195 (Aug.) 1918.
2. Fallas, Roy: Krukenberg Tumor of the Ovary, with Report of Two Cases, Surg., Gynec. & Obst. **49**: 638 (Nov.) 1929.
3. Enzer, Norbert: Krukenberg Tumors of the Ovary, Ann. Surg. **92**: 140 (July) 1930.

Wagner [4] decides that "the picture of so-called Krukenberg ovarian tumor is due to the mucoid degeneration of epithelial cells in a scirrhous carcinoma of the ovary (whether primary or secondary to a carcinoma of the stomach)."

Matters [5] says that Erdheim and Schiller have shown the Krukenberg tumor to be a pure carcinoma and always secondary to carcinoma of the gastro-intestinal tract or of the gallbladder. The cancer cells from these parts are said to fall on the ovary and to become implanted there but, being secreting cells, they continue to produce secretion and become distended, as there is no gland lumen into which to pour their secretion. The cells invade the ovary in small groups or in a diffuse manner. The cell, distended by its own secretion, pushes the nucleus to one side, flattening it against the side wall and producing the well known signet ring described by Krukenberg. The presence of these distended cells markedly irritates the connective tissue of the ovary and so stimulates it as to produce the appearance of a fibrosarcoma.

In the discussion of Miller's [6] report of a case, J. F. Browne of Edinburgh suggested "the possibility of three types of tumors producing the microscopic appearance found in Krukenberg tumor. In one they may be entirely sarcoma, the signet ring cells being derived either from spindle cells or from round cells. In the second possibility they could be entirely carcinomatous, the signet ring cells arising from mucinous degeneration of the cancer cells. In the third possibility both carcinoma and sarcoma may be present, the carcinoma being secondary to a tumor outside the pelvis. It has been shown that a carcinoma transplanted in rats can produce a sarcomatous change in the connective tissue of the host. One can conceive of no more favorable location for the stimulation of such a growth than in the ovary, where the stroma has such a peculiarly embryonic character and therefore might be supposed to be especially liable to such malignant properties."

TABLE 2.—*Organs Involved in the Sixty-Eight Cases That Show Lesions Other Than in the Ovary*

Organs	Frequency of Involvement
Stomach	54 cases
Small intestine	5 cases
Appendix	2 cases
Sigmoid	4 cases
Rectum	2 cases
Remainder of colon	5 cases
Gallbladder	1 case
Liver	2 cases
Spleen	1 case
Omentum	2 cases
Uterus	4 cases
Ureter	1 case
Breast	2 cases
Lungs	1 case
Bone	1 case
Dura	1 case

Jarcho [7] believes that he "has been able to follow the course of travel of cancer cells through the lymphatics to the ovary."

In March 1925 Miller [6] stated that "no papers have yet been published that would dogmatically state the explanation of the peculiar structures of the Krukenberg tumor. The majority of cases would point to the theory that it is usually secondary to a carcinoma of the gastro-intestinal tract."

Miner [8] reported a case that looked like one of primary unilateral Krukenberg tumor one year after operation in a woman, aged 19. The report that was made, Nov. 23, 1933, shows that this woman is alive and well and has become the mother of three healthy children since the operation. Dr. Miner submitted the slides obtained from this case to a number of pathologists for opinions. Some diagnosed it a Krukenberg tumor, some claimed it to be a follicular carcinoma and some a sarcoma. It is likely that it was not a Krukenberg tumor.

Greenhill [9] reported an operation on a patient in October 1930 in which all tests to determine a primary lesion in the gastro-intestinal tract have been fruitless. The patient died two months after operation without autopsy.

Why is it necessary that the ovarian picture must always be a secondary one? Cannot a carcinoma of the same type originate in the ovary primarily in some certain cases and by its presence stimulate the connective tissue cells of the ovary to the same growth that is produced by a carcinoma originating in the stomach and secondarily involving the ovary?

This surely can be possible and would readily explain the cases in which no carcinoma has been found in other abdominal organs. True, gastro-intestinal carcinoma has been found in most of the cases that have come to autopsy, but there are a few remaining in which there is reasonable certainty that only the ovary was involved. Wagner [4] concurs in this view.

It is very evident from table 2 that, in the cases reported in which the data have been sufficiently accurate and definite to determine the location of lesions, most of the cases have presented an involvement of the gastro-intestinal tract. Some cases showed lesions in a number of organs.

Many of the recorded cases did not come to autopsy and therefore did not reveal a list of the organs involved. The sixty-eight cases (table 2) selected out of the ninety-one studied did give records sufficiently complete to plan the diagram. These observations make this tumor as important to the gastro-enterologist as to the gynecologist.

The case that I report invites the attention of the proctologist to this tumor, making it a differential diagnostic problem in strictures of the rectum.

REPORT OF CASE

Mrs. H. S., aged 64, white, had had attacks of pain in the epigastrium and right hypochondrium for several years, associated with nausea, vomiting, anorhexia and weakness. At the examination, April 22, 1931, the examiner noted a sensation of a mass in the epigastrium which was firm and somewhat tender. He diagnosed carcinoma of the stomach or gallbladder disease.

Four months later, in August, at which time she first came under my observation, she had frequent attacks of diarrhea with some incontinence. At times she could control the sphincter and at others she had no control.

She was admitted to the hospital and a marked constriction of the rectum was found, starting about 3 inches above the anus, through which the finger could not be passed. The wall was fairly smooth and superficially ulcerated with some small nodular swellings at the lower end of the stricture. One of the nodules was removed for examination; a report was made that there was inflammatory mucous membrane but no malig-

4. Wagner, G. A.: The Histogenesis of the So-Called Krukenberg Ovarian Tumors, Wien. klin. Wchnschr. **15**: 519, 1902.
5. Matters, R. F.: Ovarian Malignancy, with Special Reference to Krukenberg Tumors, M. J. Australia **1**: 181 (Feb. 13) 1926.
6. Miller, Douglas: Report of Two Cases of Krukenberg Tumor of the Ovary, Edinburgh M. J. **32**: 46 (March) 1925.
7. Jarcho, Julius: Krukenberg Tumors and Their Practical Problems, Am. J. Obst. & Gynec. **13**: 288-307 (March) 1927.
8. Miner, Donald: Primary Krukenberg Carcinoma of the Ovary, S. Clin. North America **6**: 1645, 1926.
9. Greenhill, J. P.: Krukenberg Tumor, Am. J. Obst. & Gynec. **22**: 445 (Sept.) 1931.

nant condition. A vaginal examination was not made. The blood Wassermann reaction was negative. Examination of the blood showed secondary anemia. The stricture was gently dilated and a blood transfusion was given, after which the patient improved in weight and strength and the diarrhea lessened. There were no gastric or pelvic symptoms during this period, no abdominal distention and no palpable mass in the epigastrium. The patient was discharged from the hospital in November. Rectal bougies were passed regularly to maintain a fair degree of comfort.

In July 1932 she came to the hospital again with more constriction of the rectum and an increasing anemia. Transfusions improved the blood picture and a Jelks operation for relief of the stricture was done, after which she had greater comfort, leaving the hospital again, August 29.

November 17, severe paroxysmal abdominal pains, distention and prostration suddenly developed. She was brought to the hospital and the abdomen was opened five hours after the pain started. There was some fluid in the abdomen; a rupture was found in the upper part of the sigmoid, the edge of the hole being necrotic. This rent was sutured. At this time numerous hardened whitish plaques were noted in various places on the small bowel, and in the ileum there was a markedly constricted area about 1 to 2 inches long with great dilatation above and below it, making it resemble an hour glass. The appendix

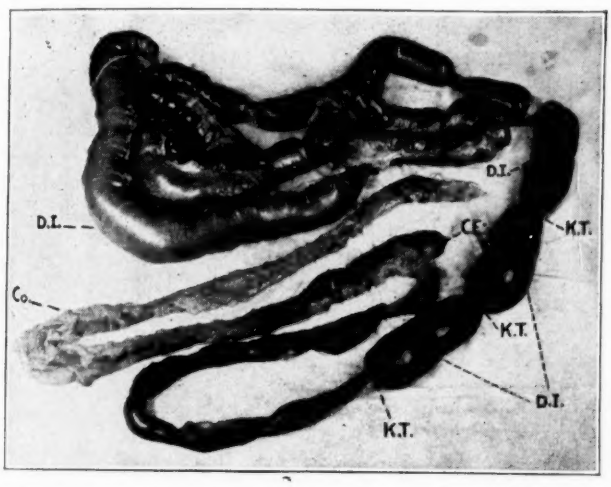

Fig. 1.—Krukenberg tumor, showing the ileum and colon involvement: *K. T.* shows successive points of constriction of the ileum due to tumor infiltration about 50 cm. above the cecum. *D. I.*, dilated ileum; *Co.*, colon; *CE.*, cecum.

was seen to be involved in a definite hardening process. The walls were extremely thick and firm, making it look like a frankfurter. This induration extended slightly into the cecum. The appendix was removed for diagnostic purposes. Both ovaries were found enlarged but were not removed. There was a myoma on the uterus. The remainder of the abdomen was not explored, for obvious reasons.

The patient died on the sixth day after operation.

POSTMORTEM EXAMINATION

Postmortem examination, performed by Dr. Frederick Light of the Pathological Department of the Reading Hospital, showed in part the following:

Stomach.—The stomach was rather small and measured 21 by 7.5 cm. when opened. The pylorus was much thickened for a distance of 7 cm. and the wall in this area was 1.5 cm. in thickness. It was quite tough and cut with greatly increased resistance. In the fundus there were elevated patches in the mucosa which averaged 1 to 2 cm. in diameter. The remainder of the gastric wall varied from 0.5 to 1 cm. in thickness.

Section from the pylorus showed the usual thick circular layer of muscularis. The submucosa and the mucosa were greatly thickened. The mucosal glands, instead of lying closely side by side with only a little intervening stroma, were widely separated one from another, the tunica propria being much heavier than normal. The extensive thickening of the mucosa and submucosa was seen to be the result of the presence of large numbers of peculiar cells. These were large oval cells with an abundant acidophilic cytoplasm. The nucleus in some was oval and lay centrally. In others the nucleus was crescent shaped and was pressed against the rim of the cell. In these signet ring cells, the cytoplasm tended to be clearer and the cell margin became circular. Between these two extreme kinds of cells, all degrees of variation could be demonstrated. These tumor cells had no pattern of any sort but were scattered about at random, in the manner of an infiltration. A good many lymphocytes were also present. The tumor cells were limited

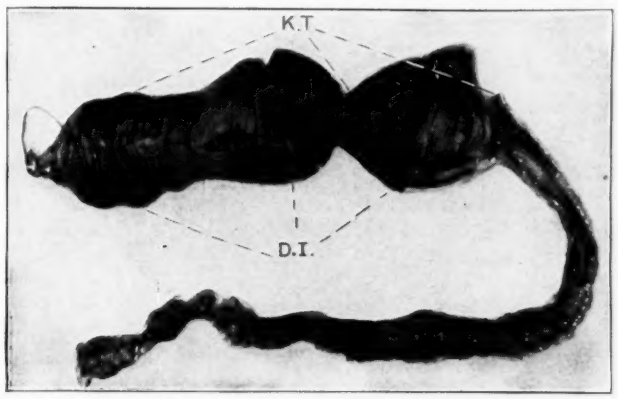

Fig. 2.—Krukenberg tumor with bowel opened, showing points of constriction by the tumor, *K. T.*, and of the dilated ileum, *D. I.*

almost entirely to the mucosa and submucosa, only a few being found in the muscularis. A few, however, could be found even in the outer muscular layer.

Ileum.—Approximately 50 cm. above the cecum was a tubular constriction of the ileum which extended for a distance of 16 cm. At this point the wall of the intestine was greatly thickened. It was above this point that the intestine was distended and bluish. Below this point the intestine was small, practically empty and grayish.

In the middle of the thickened segment the microscopic appearance was similar to that described in the stomach. The

Fig. 3.—Section of stomach under low power, showing the mucosa and a portion of the infiltrating tumor.

submucosa and mucosa were heavily infiltrated with tumor cells, most of which were of the signet ring variety. The glands were widely separated from one another by the thickened tunica propria. At the border of the thickened segment the mucosa retained its usual configuration, although there was some hemorrhage into the tunica propria, also; however, there was some infiltration of tumor cells into the subserosa.

Appendix.—The specimen weighed 6.5 Gm., measured 5 cm. in length, and averaged 1.2 cm. in diameter. The serosa

appeared smooth and glistening, with no gross evidence of a deposit of any exudate. The surface vessels were markedly injected over the entire surface, giving the specimen a fairly even red color externally. A fatty meso-appendix was attached throughout the entire length of the specimen. The organ was tough, firm and not at all pliable. When the specimen was sectioned, the cut surface bulged beyond the serosa. There was no differentiation between muscularis and mucosa on cross section, and the lumen was entirely obliterated to the most

Fig. 4.—Section of stomach under low power, showing the submucosa and a portion of the muscular layer infiltrated with tumor cells.

distal part of the organ. Just within the serosa was a ring of white tissue 2.5 cm. in thickness. This was distinguishable from a central core of yellowish tissue, which probably occupied the area of the former lumen. This central core measured 5.5 cm. in diameter.

This organ was removed at operation ante mortem and presented as a biopsy specimen. The subserosal tissues were edematous and bore a round cell infiltration. The muscularis was of normal thickness. The lumen and mucosal epithelium

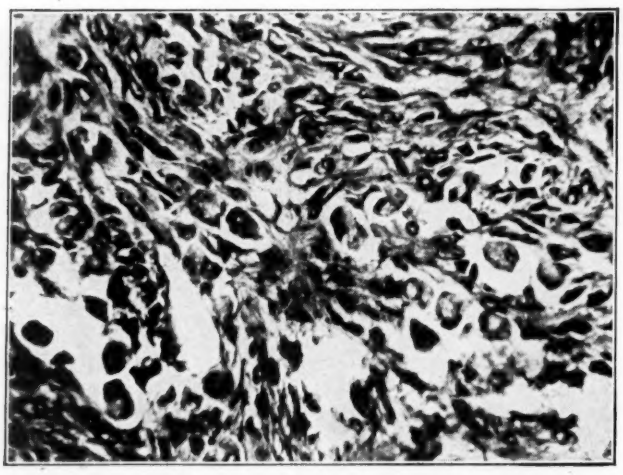

Fig. 5.—Section of stomach under high power, showing the characteristic "signet ring" cells with compressed nuclei on the edge of the protoplasm.

were absent, a few small lymphoid follicles marking the site of the former lumen. The submucosa was tremendously thickened, accounting for about half the cross sectional area. Here again, in addition to the deposition of fibrous tissue, there was an infiltration of tumor cells, a few of which were of a typical "signet ring" type.

Sigmoid and Rectum.—The rectum was adherent to the uterine masses posteriorly. Its lumen was much constricted, measuring only 3 cm. in circumference. The rectal wall was very tough and measured 1.5 cm. in thickness, and its mucosa was edematous and rugosed.

Sections of the sigmoid were from near the site of the perforation. The microscopic picture was similar to that of the stomach. The submucosa and mucosa were densely infiltrated with lymphocytes and tumor cells and there was some invasion of the muscularis. Scattered typical colonic glands were found, with abundant goblet cells.

Uterus.—This measured 8 by 4.5 by 4 cm. and its wall was 2 cm. thick. There was a subserous fibroid at the fundus which measured 4.5 by 3.5 by 3.5 cm. It was well encapsulated and, on section, it was gray and showed whorls of tissue.

The small tumor mass in the uterus was composed of interlacing bundles of smooth muscle and fibrous tissue. No tumor cells such as those present in the stomach and ovaries were present here.

Ovaries.—The tubes were slightly thickened and adherent to the enlarged ovaries. The ovaries were replaced by tumor masses. There were two masses in the right ovary which were adherent to one another. The one measured 8 by 5 by 3 cm. and the other 6.5 by 3 by 2 cm. The smaller mass had a central cyst 1.2 cm. in diameter and contained clear fluid. The tumor mass in the left ovary measured 7.5 by 4 by 3 cm. All these masses were adherent to the pelvic wall, and all presented the same general appearance. All of them had a

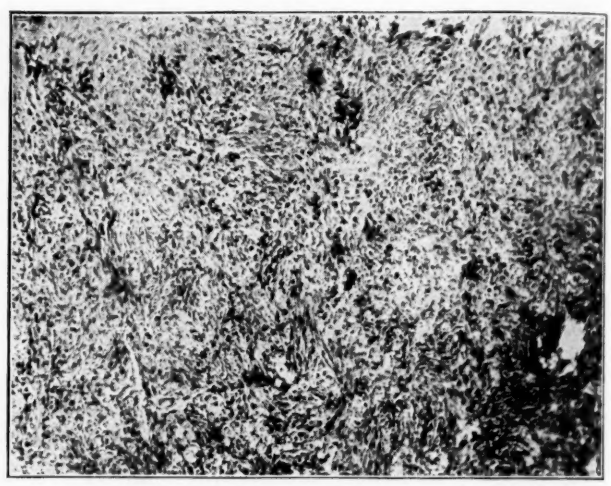

Fig. 6.—Section of the ovarian tumor under low power, showing many groups of the carcinomatous cells.

smooth external surface. The cut surface was smooth and grayish white and had a lobulated appearance along the periphery that measured 2 cm. in width, and a central core that was gray and much firmer.

In the thickened peripheral parts of the ovaries the sections showed the stroma to be very heavily and diffusely infiltrated with tumor cells. They occurred in small groups separated from one another by a few stromal cells. The signet ring cells predominated here, producing the typical picture of a Krukenberg tumor. The microscopic appearance was quite uniform throughout both ovaries.

The diagnosis was Krukenberg tumor involving the stomach, ileum, appendix, sigmoid, rectum and ovaries.

This case apparently started with symptoms of stomach dysfunction as early as April 1931, at which time the physician suspected carcinoma. The x-rays at this time showed no evidence of a malignant growth, although even this early the stomach was undoubtedly involved in the process that was later found at autopsy.

The next picture was one of rectal stricture with ulceration, found when an attempt was made to determine the cause of frequent bowel movements with incontinence. This stricture resembled the lesion found in lymphopathia venereum or in gonorrheal infection. There were no symptoms at this time suggesting ovarian

involvement, or they were completely overshadowed by the rectal distress. The rupture of the sigmoid furnished the opportunity to see the pathologic condition of the intestine and ovary, which suggested the probable diagnosis.

This case strongly suggests that the primary lesion was in the stomach, with metastases to the small intestine, appendix, sigmoid, rectum and ovaries.

The distribution of lesions in this case would suggest its having been spread by the cancer cells falling from the stomach focus into the organs of the abdomen and becoming implanted there as suggested by Erdheim and Schiller.[10] The abdomen looked as if it might have been subjected to a spray of metastatic cells.

It somewhat resembled one case reported by Major in that numerous small, hard, elevated whitish plaques were noted on the wall of the stomach and intestine. Like his, my case was noted for the great amount of fibrous tissue found in many of the lesions of the stomach and intestine.

Krukenberg tumors with rectal involvement have been very rare and only a few have been found in the

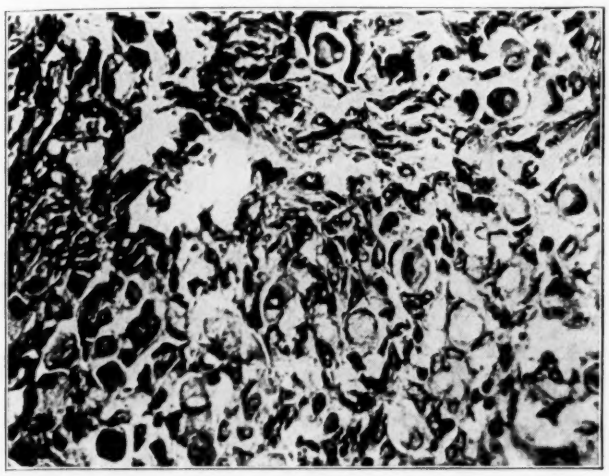

Fig. 7.—Section of the ovary under high power, showing clearly the large polyhedral and rounded cells with mucoid contents pushing the nuclei to one side, giving the "signet ring" appearance.

literature. Jarcho reported a case in which there was a mass of tumor tissue in the pelvis involving the left ureter, ileum, uterus and rectum. This rectal involvement was apparently only a part of a late tumor growth into it from other pelvic organs and not a separate rectal infiltration. Hundley[11] cites a report of Frankl's in which the occurrence of three ovarian tumors of the Krukenberg type were noted, one originating in the rectum and two in the lower part of the sigmoid. This one case of Frankl's seems to be a definite rectal involvement of a Krukenberg tumor.

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ABSTRACT OF DISCUSSION

DR. JOSEPH COLT BLOODGOOD, Baltimore: More papers of this kind are needed. This paper brings to the reader practically all existing knowledge of this remarkable intra-abdominal malignant disease. It illustrates the value of frozen sections in the operating room so that the operator can be informed at any moment and at frequent intervals as to the exact condition with which he is dealing. It also shows that when a surgeon removes a tumor of an ovary he should know its nature at once. When there is no possibility of a frozen section, the stomach should be at least palpated from the pelvic laparotomy wound. Trained pathologists in the operating room during operations are just as important as trained anesthetists. This paper brings the subject of Krukenberg tumors down to date.

DR. HARRY E. BACON, Philadelphia: In two cases of Krukenberg tumor, one of which is from a series of four collected by Dr. Gault of Temple University, the initial symptoms were referable to the sigmoid and rectum. A woman, aged

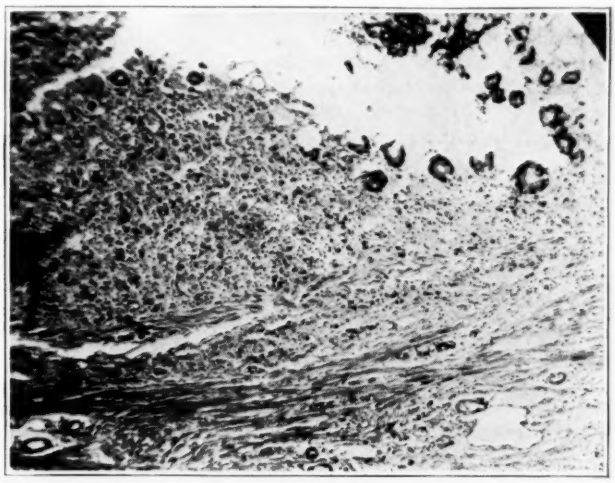

Fig. 8.—Section of the sigmoid under low power, showing the tumor infiltrating the various coats.

25, was admitted to the University Hospital in November 1930 because of nausea and vomiting. Four days later she was discharged. In June 1931 she returned complaining of pain in the rectum and frequent stools. A diagnosis was made of rectal stricture, and a colostomy was performed. In December the patient was admitted to the Philadelphia General Hospital, at which time rectal examination elicited an irregular constricting mass about 4 inches above the anal margin. The patient succumbed three months later. The necropsy showed the intestine bound together and adherent

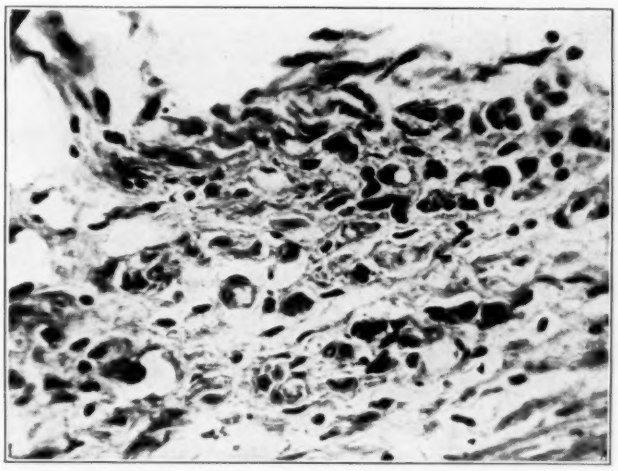

Fig. 9.—Section of the sigmoid under high power, showing a portion of the submucosa infiltrated with tumor cells and lymphocytes.

to the pelvic organs. The left ovary was enlarged, firm and nodular. In the constriction of the sigmoid there seemed to be a generalized thickening of the serous coat. Lymph nodes of the mesentery and some of the retroperitoneal glands were enlarged but were soft and grayish pink. On the left side of the pelvic peritoneum were hundreds of small areas from 1 to 2 mm. in diameter in the subserosa. In the stomach was a diffuse infiltrating growth involving the subserosa, muscular and submucous coats, with great increase in the thickness of the wall, which resembled grossly a diffuse scirrhous car-

10. Cited by Matters.[5]
11. Hundley, J. M. Jr.: Krukenberg Tumors and Other Secondary Ovarian Carcinomas, South. M. J. **24**: 579 (July) 1931.

cinoma (linitis plastica). The other case was that of a Negro woman, aged 41, who was referred to the proctologic clinic. She had an abscess three months before, which was lanced by her family physician and after which a discharge of pus was noted intermittently. On examination, an anorectal fistula was present. Digital examination elicited two small papillae and a circumscribed area one-half inch above the anorectal line and slightly to the left of the anterior rectal wall. The tract was excised after the internal opening had been located. The area that was thought to be inflammatory now appeared as a nodule the size of a small cherry, beneath the mucous membrane and located in the rectovaginal septum about three-fourths inch above the anorectal line. The nodule was smooth and firm. The histopathologic picture was that of a Krukenberg tumor. In checking the history, it was found that in December 1932 the appendix, right tube and ovary, had been removed. The latter was cystic. In April of the same year the patient had been operated on and a small growth found on the greater curvature of the stomach close to the pylorus. The laboratory reported carcinoma. This case is unusual. The diagnosis was initially made from the rectum. It is interesting that this patient appears healthy and free from any complaint.

DR. JULIUS FRIEDENWALD, Baltimore: In the study of cases of leather-bottle stomach or sclerosing carcinoma, the so-called linitis plastica, the histologic examination presents numerous small cells containing irregular nuclei of varying size observed especially in the submucosa in addition to nucleated connective tissue cells. These cells may occur singly or in groups and resemble epithelial cells. The cytoplasm of these cells is usually clear, with no distinct membrane and frequently large vacuoli. The vacuolated elements frequently have their nucleus pushed to the periphery, presenting the appearance of a signet ring. The cells are found in the submucosa, in the connective tissue of the muscularis especially in the areas surrounding the blood vessels. The nature of these cells has not as yet been definitely determined, but attention has been directed to them as suggestive of the epithelial cells found in the Krukenberg carcinoma. While it has been established that the linitis plastica or sclerosing carcinoma is commonly observed in males and the Krukenberg tumor only in females, the microscopic appearance of the two growths is usually quite similar, and the question arises as to whether the two are related. A number of pathologists who were consulted regarding this question were unable to give any definite decision in this respect. I am anxious to learn whether Dr. Runyeon has been able to collect any data regarding the question of relationship. The histologic similarity would seem to point in this direction and Dr. Bacon's first case rather confirms this.

DR. F. G. RUNYEON, Reading, Pa.: In answer to Dr. Friedenwald's question, I have not thought of the relation between these two conditions, but the stomach in my case was really a typical leather-bottle stomach. The pathologist noted it and felt it was exactly that type of stomach and resembled the one reported by Dr. Miller. I presented this paper particularly to report another case of Krukenberg tumor a little unusual in its distribution and to draw the attention of the gastroenterologist and proctologist to it on account of the possibility of their running into this type of case and probably not thinking, because it is so unusual in the literature, that it might be a Krukenberg tumor.

Case Histories and Emotional Factors.—When we consider, too, what a large and increasing proportion of our patients is suffering from purely functional disorders, the scarcity, in most histories, of information regarding possible emotional factors is often surprising. This is not entirely the interne's fault in many cases; the trouble is more deep-seated than that. The curricula of our medical schools are still mainly arranged to cover the study of the physical aspects of disease, and in our hospitals and dispensaries, where our future internes are trained, the mental factors, which may be the dominant ones in the production of the clinical picture, often receive scant notice.—Blumer, George: Some Discursive Remarks on Bedside Diagnosis, *Yale J. Biol. & Med.* **6**:571 (July) 1934.

THE PROBLEM OF RADIOSENSITIVITY

MAX CUTLER, M.D.

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CHICAGO

The introduction and development of radium and x-rays as therapeutic agents in cancer has raised pertinent questions concerning the radiosensitivity of normal and neoplastic cells, which have assumed both a theoretical interest and practical importance. These problems concern the pathologist, surgeon and radiologist alike, for each is called on to render important decisions on the treatment of cancer, which involve an intimate knowledge of the established principles of radiosensitivity.

It is my purpose in this communication to present a critical summary of some of the biologic, pathologic and clinical knowledge of radiosensitivity so far as it applies to the practical problems of the treatment of cancer.

An immense literature has accumulated on this subject and much of the evidence presented is both confusing and conflicting. Some of the reasons for the state of confusion are at once obvious. Perhaps the most important is the fact that the science of radiation is relatively new. Following the discovery of x-rays and radium only about thirty-five years ago, the problem passed through a preliminary experimental period

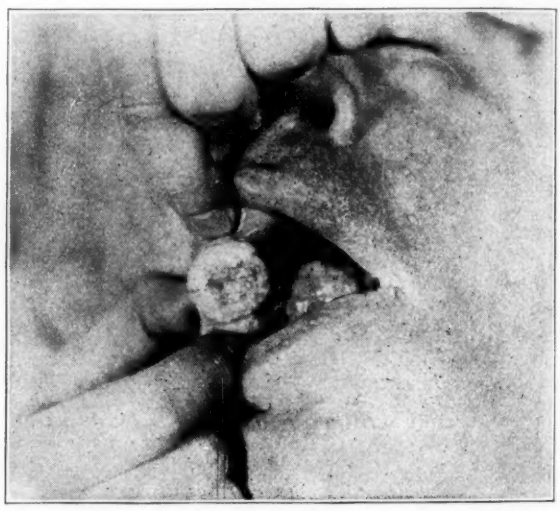

Fig. 1.—Squamous carcinoma of the mucous membrane of the cheek, before treatment.

of physical and biologic studies that were essential to establish the fundamental basis of radiotherapy; and although the clinical application of radium and x-rays began about thirty years ago, physicians are today only beginning to approach an understanding of some of the principles of radiotherapy and their clinical application to the treatment of cancer. And so it is no simple task to elicit from the mass of data that exist in the literature that small portion which has stood the test of time from the vast amount of data that in the light of present knowledge must be discarded.

No more striking example of the rapidly changing conceptions can be presented than the question of the radiosensitivity of squamous carcinoma. With the

Read before the Section on Pathology and Physiology at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 13, 1934.

exception of the French school, most workers have recorded that squamous carcinoma is a radioresistant tumor. The discrepancy was soon discovered to be entirely a matter of technic and dosage. Squamous carcinoma was designated as a radioresistant tumor at a time when a short, intense and inadequate exposure to x-rays or radium failed to sterilize it until Regaud [1] and his collaborators in Paris and Pfahler [2] in America established that, by protracting the treatment over a period of days, the normal tissues can withstand much greater doses, and this change in technic has resulted in making it possible to sterilize squamous carcinoma. With present methods, squamous carcinoma fulfils all the criteria of the definition of a radiosensitive tumor, but this fact is not known to many pathologists and clinicians. I have witnessed repeated instances in which thoroughly competent pathologists designate squamous carcinoma as radioresistant and equally excellent surgeons decide on the basis of such reports to perform surgical removal of a lesion that is amenable to radiation and in which present knowledge indicates radiotherapy to be the method of choice. It cannot be overemphasized that the pathologist who undertakes to express an opinion on the radiosensitivity of a tumor is assuming a grave responsibility, because the surgeon who may not be completely familiar with these matters frequently bases important decisions of treatment on such information. It is the duty of the pathologist, therefore, before passing judgment on radiosensitivity, to become thoroughly familiar not only with the established principles of radiosensitivity but also with the modern advances on this subject. That the microscopic structure of a tumor is only one of a group of factors which indicate the property and degree of radiosensitivity is now fully established. An estimate of radiosensitivity in relation to treatment can therefore be made only in consultation between the pathologist and the radiotherapeutist if erroneous and misleading deductions are to be avoided.

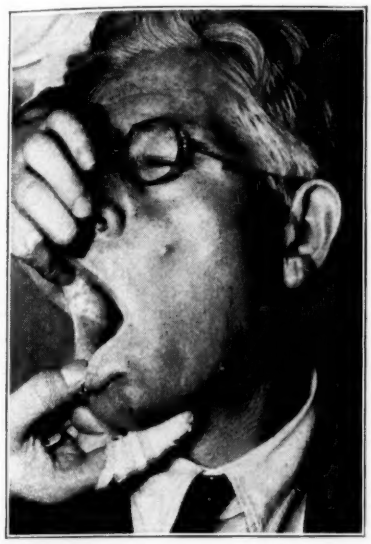

Fig. 2.—Same case as in figure 1 after treatment, illustrating principle of selective irradiation (sterilization of the lesion without necrosis).

Important as are the advances that have been made in the past in the physics of x-rays and radium and in the technic of application of these agents, an even more important field of investigation has developed which deals with the physiologic and biologic effects produced in normal and neoplastic tissues that are exposed to these agents. This field of study deals with radiophysiologic principles and attempts to explain the method by which irradiation effects the disappearance of tumor cells and at the same time preserves the normal structures.

For a period of years, studies have been made of gross and microscopic specimens of tumors removed after various forms of radiation with a special view of correlating morphologic structure with radiosensitivity and also to estimate the changes produced in tissues following their exposure to different technics and various doses of x-rays and radium. The observations of many workers along these lines constitute a source of basic information on the problem of radiosensitivity. However, it is quite evident that the response of tumors to irradiation is governed by a group of factors including physical, histologic, physiologic, pathologic and clinical, which in combination with one another determine the ultimate result. The failure to recognize the relative importance of all the principles that influence the ultimate result may lead to errors in interpretation of radiophysiologic phenomena.

In passing from purely laboratory investigations to clinical observation of lesions under the influence of radiation therapy, it soon becomes obvious that a complete understanding of the problem of radiosensitivity is quite impossible without thorough familiarity with tumors before, during and after their exposure to these agents and that the ultimate criterion and only absolute test of the radiosensitivity of a tumor is its clinical behavior. Thus, clinical observation records numerous examples of marked radioresistance in tumors which, according to microscopic study, should prove to be highly radiosensitive, and with equal frequency, a high degree of radiosensitivity may be observed when all the histologic factors indicate the presence of a radioresistant lesion. These observations emphasize the inadequacy of microscopic studies alone to predict the response of tumors to radiation therapy. The explanation for these apparent exceptions is in the present state of knowledge not forthcoming. There is considerable evidence that physiologic phenomena as, for example, the function of secretion, affect these results and no doubt radiosensitivity is influenced by biologic factors that give no microscopic evidence of their presence.

Fig. 3.—Squamous carcinoma of the mucous membrane of the cheek following incorrect interstitial irradiation, illustrating the principle of caustic irradiation with the production of radionecrosis.

A decision on the choice between operation and irradiation in the treatment of a given tumor is at times

1. Regaud, C.: Radiophys. et radiothérapie **1**: 443, 1930; Acta radiol. **11**: 455, 1930.
2. Pfahler, G. E.: Surg., Gynec. & Obst. **41**: 443 (Oct.) 1925.

exceedingly difficult. In many examples this decision must be based on two factors: operability and radiosensitivity. Unfortunately, the clinical signs of operability are attended by gross inaccuracies and the arbitrary division of neoplasms into operable and inoperable groups is subject to numerous fallacies. The inability to judge the extent of disease by clinical examination constitutes perhaps the most important single source of fallacy in the statistical studies of cancer.

Fig. 4.—Squamous carcinoma of the penis before treatment.

As to the results that may be expected from radiation, adequate clinical experience, pathologic data and experimental investigations are available to indicate on the one hand the value of radiation therapy and on the other hand the limitations of these agents in the treatment of neoplastic disease. Of the several factors that determine the success or failure in the radiotherapy of a given tumor, the factor of radiosensitivity is the most important.

A radiosensitive tumor may be defined as one that can be completely destroyed by a correct irradiation without permanent damage to the surrounding normal structures.

The complete sterilization of a tumor by radiation can be accomplished in two ways: (1) selective radiation and (2) caustic radiation.

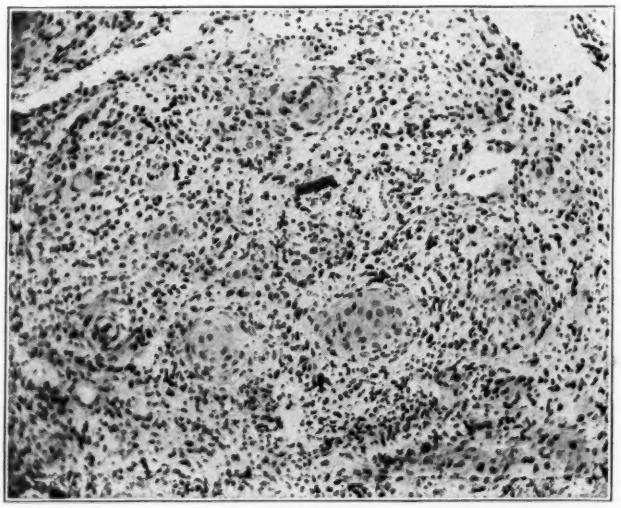

Fig. 5.—Section of lesion shown in figure 4, showing adult squamous carcinoma.

Selective radiation—the ideal form of radiotherapy—sterilizes cancer cells without causing serious damage to the surrounding normal structures. As Regaud has pointed out, this result is possible only when some difference exists between the radiosensitivity of the cancer cells and that of the surrounding normal cells. Those tumors which possess this property are called radiosensitive. Most tumors fail to qualify under this principle and must be classed as radioresistant. The selectivity of radiation in the treatment of radiosensitive tumors is the underlying principle of radiotherapy and it is this factor that differentiates radium and x-rays from such methods as electrocoagulation, in which no specific or selective effect on tumor cells can be demonstrated.

Caustic radiation differs from selective radiation in that it not only destroys the tumor but seriously injures the surrounding normal tissues. This form of radiotherapy has a limited field of usefulness and is specially applicable to the treatment of the more radioresistant tumors that are not too extensive. Nonselective or caustic irradiation of radioresistant tumors when the lesion is extensive usually results in radionecrosis with sloughing, secondary infection and local recurrence. The constant aim in radiotherapy is to devise methods by which complete sterilization of a neoplasm may be effected without radionecrosis.

There are no reasons for assuming that a given tumor is equally resistant to radiation throughout its life history. On the contrary there is considerable evidence to indicate that tumors pass through alternating periods of radioresistance and radiosensitivity. Undoubtedly changes in metabolism influence response to radiation; thus Crabtree and Cramer [3] have discovered recently that exposure of tumor tissues to low temperatures greatly increases the susceptibility to radium, whereas anaerobiosis results in greatly increased resistance. The results of these investigations also indicate that the biologic effect of radiation is not produced through an action on the glycolytic mechanism. These results are at variance with Packard's [4] experiments with Diosophila eggs, which indicated that lowering the metabolic rate by lowering the temperature diminished the susceptibility to radiation. Ewing [5] is of the opinion that the intrinsic property of the cells of origin more than any other factor determines the property of radiosensitivity, and there is much evidence to support this contention. Regaud has observed that the property of secretion is antagonistic to the property of radiosensitivity and believes that the radioresistance of adenocarcinomas is possibly to be explained on this basis.

Fig. 6.—Squamous carcinoma of the penis after surface irradiation, illustrating radiosensitivity of squamous carcinoma by protracted and adequate surface irradiation.

From time to time efforts have been made to influence the property of radiosensitivity. In 1909 Schwartz [6] used compression and cooling of the tissues and in 1924 Jolly [7] noted increased radioresistance following temporary ligation of the blood supply to certain organs exposed to radiation. Heating the tissues

3. Crabtree and Cramer: Proc. Roy. Soc. London sec. B **113**: 238, 1933.
4. Packard, Charles: J. Cancer Research **11**: 282 (Oct.) 1927.
5. Ewing, J.: Radiology **13**: 313 (Oct.) 1929.
6. Schwartz, G.: München med. Wchnschr. **56**: 1217, 1909.
7. Jolly, J.: Compt. rend. Soc. de biol. **91**: 532 (July 25) 1924.

appeared to increase radiosensitivity. The introduction of some of the heavy metals such as colloidal lead has been suspected of increasing radiosensitivity of tissues, but in none of these observations has a specific effect on the neoplastic cells been demonstrated and clinical results have been equally unsatisfactory.

ESTIMATE OF RADIOSENSITIVITY

The degree of radiosensitivity of a tumor may be estimated after a consideration of certain clinical and pathologic factors. It is now fully established that the

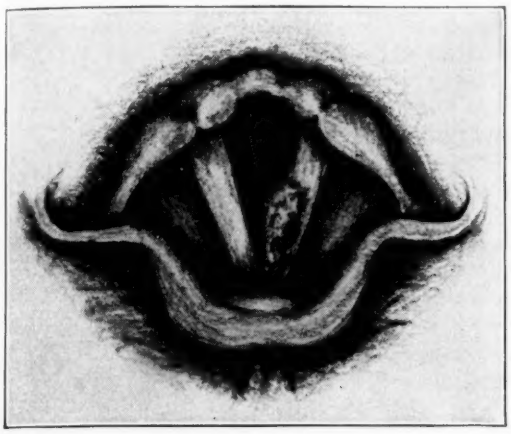

Fig. 7.—Squamous carcinoma of the right vocal cord before treatment. See figure 8.

carcinomas arising from the epidermoid structures of the skin and the mucous membrane comply with the criteria of radiosensitivity. Thus epidermoid carcinoma of the skin, lip, oral cavity, including the tongue, tonsil, sinuses, pharynx and larynx, also epidermoid carcinoma of the vagina and cervix are classed as radiosensitive. The marked radiosensitivity of lymphosarcoma and the cellular forms of Hodgkin's disease and embryonal carcinomas are well known. In contradistinction to these lesions, outstanding examples of radioresistant tumors are adenocarcinoma, melanoma, fibrosarcoma and osteogenic sarcoma. Carcinoma of the breast possesses an intermediate degree of radiosensitivity.

Within the group of epidermoid carcinomas there exist notable variations in radiosensitivity. Thus the more adult, hornifying squamous form with pearl formation is more radioresistant than the nonsquamous or transitional cell type. Lympho-epithelioma, the precise histogenesis of which is not known with certainty, is highly radiosensitive. Not infrequently mixed histologic types are encountered with one or another type of cell predominating. This fact must be considered in attempting to estimate radiosensitivity from a study of small biopsy specimens.

It should be emphasized that radiosensitivity does not necessarily indicate curability, nor should radioresistance be taken to imply incurability. Thus, for example, a localized radioresistant but papillary adenocarcinoma may be caused to disappear without radionecrosis under intensive irradiation approaching a caustic dose and the patient may remain cured of the disease. Such a result is exceptional, but enough examples of this kind are available to prove the point. On the contrary, a highly radiosensitive tumor as, for example, lympho-epithelioma of the tonsil, may disappear with dramatic rapidity when the course of radiation has been only partly administered, and the patient may die promptly of distant metastases.

Notable exceptions to the radioresistance of glandular carcinomas are encountered in malignant tumors of the thyroid, which not infrequently exhibit favorable response to radiation therapy in spite of the fact that the histologic structure indicates radioresistance according to the usual microscopic criteria.

In estimating radiosensitivity, one may consider a tumor radiosensitive when a correct maximum surface irradiation can accomplish a complete sterilization of the local lesion without permanent serious damage to the tumor bed; i. e., without radionecrosis. The complication of metastasis should not be considered in this connection, as that event is dependent on other factors entirely unrelated to the problem of local radiosensitivity.

I have been impressed repeatedly by the radiosensitivity of lesions that are papillary although the histologic structure may indicate a state of radioresistance. I have observed several examples in which papillary adenoma malignum of the rectum has disappeared under intense external radium therapy and early papillary adenocarcinoma of the rectum has undergone complete regression (no recurrence after three years) under surface radium therapy and massive external radiation, yet I have never observed the complete disappearance of lesions of a similar histologic structure when they have infiltrated deeply the underlying structures. I am strongly of the opinion, therefore, that the gross character of the lesion, more particularly its papillary or infiltrating character, may be under certain circumstances a more important guide to radiosensitivity than the microscopic appearance of the growth. The ability to eradicate superficial papillary

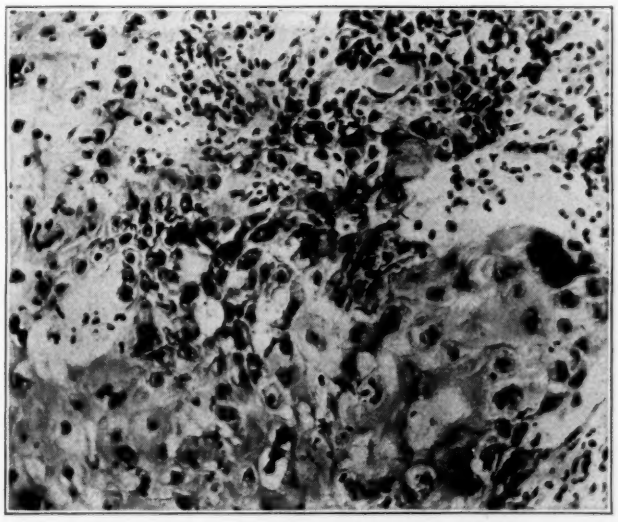

Fig. 8.—Section showing squamous carcinoma of the larynx shown in figure 7. Sterilization of the lesion was accomplished by external irradiation, illustrating radiosensitivity of adult squamous carcinoma by protracted irradiation. The patient received 100,000 milligram hours to each side of the neck with the 4 Gm. radium pack; two treatments were given daily and consecutively for forty-one days, at 15 cm. distance. The patient has been well for two years.

adenoma or low grade adenoma malignum of the body of the uterus by intra-uterine and external radium therapy is another example of the radiosensitivity of papillary lesions. In a recent review of this subject, Stewart [8] has recorded similar observations.

8. Stewart, F. W.: Radiosensitivity of Tumors, Arch. Surg. **27**: 979 (Dec.) 1933.

The response of a tumor to radiation—the therapeutic test—remains the most accurate and certain clue to its radiosensitivity and constitutes an important guide in treatment. Thus an estimate of the radiosensitivity of a tumor may be made after a careful consideration of clinical, gross pathologic, microscopic and radiophysiologic factors.

RADIOSENSITIVE TUMORS

With the exception of the embryonal carcinomas, Hodgkin's disease and lymphosarcoma, the strictly radiosensitive tumors have been limited to epidermoid carcinomas of the skin and mucous membranes. Thus, the outstanding successes in radiation therapy have been accomplished in carcinoma of the skin, lip, tongue, oral mucous membrane, tonsil, pharynx, larynx and cervix. It has been noted that it is precisely in these locations that irradiation has largely replaced surgical procedures.

Success in the treatment of these lesions depends on numerous factors aside from their radiosensitivity. The most important of these factors are the extent of the disease and the correctness of radiation. As regards the latter factor, it is important to point out that the responsibility of the radiotherapist is far greater today than it has been in the past. As long as the radiotherapy of cancer was limited to the treatment of advanced and usually hopeless cancer, inadequate training and incomplete equipment could result only in a lesser palliation. Today the radiotherapist is confronted with the radiation treatment of certain forms of early cancer that are amenable to radiation but are also curable by surgery. When one fails to cure an early operable carcinoma by radiation, one must be prepared to defend one's position. Responsibility is far greater than it was in the treatment of palliative, hopeless cases. Several questions immediately arise: Was the case properly selected and suitable for irradiation? Was the treatment administered according to the most modern technic and by means of the most effective equipment? Was the failure due to an incorrect irradiation or was it due to the extent of the disease or possibly to an unusually high degree of malignancy of the tumor? The treatment of early cancer by radium and x-rays, therefore, involves comprehensive knowledge of clinical behavior, pathologic varieties and radiophysiologic phenomena related to tumors in order to evaluate correctly and interpret properly the successes and failures of these methods.

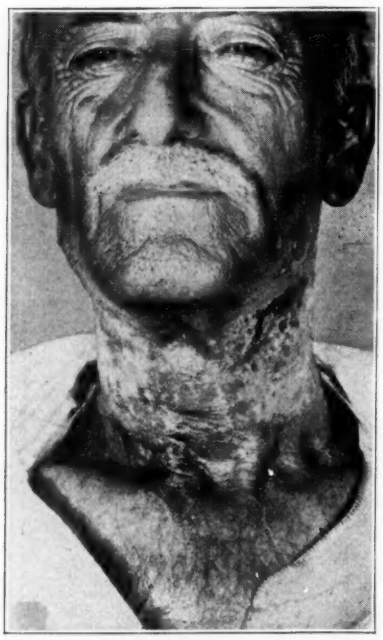

Fig. 9.—"Radio-epidermite" following radium pack therapy. A total of 200,000 milligram hours with the 4 Gm. radium pack was administered over a period of fifty days.

RADIORESISTANT TUMORS

A radioresistant tumor is one that cannot be completely sterilized without serious and permanent damage to the surrounding normal tissues. Thus it is evident that radioresistance is not necessarily synonymous with incurability by irradiation. A small, localized radioresistant lesion can be cured by an intense, caustic irradiation, but such treatment causes not only a destruction of the growth but also a radionecrosis of the tumor bed. This type of irradiation is to be avoided, because in most instances the eradication of such a neoplasm is best accomplished by surgical methods. There exist, however, a group of tumors possessing an intermediate degree of radiosensitivity in which eradication of the lesion can be accomplished by a caustic interstitial irradiation without radionecrosis. The more radioresistant forms of carcinoma of the breast are excellent examples of this type.

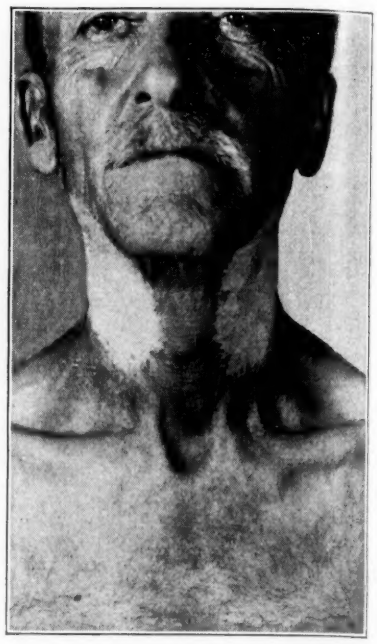

Fig. 10.—Skin healed sixty days after height of reaction.

Adenocarcinoma, melanoma, osteogenic sarcoma, fibrosarcoma and neurogenic sarcoma represent the radioresistant lesions and constitute the group that thus far has failed to respond satisfactorily to radiation therapy, but it should be pointed out that even among this group one encounters exceptions in which the relation between histologic structure and radiosensitivity fails to be maintained. Especially is this likely to occur when portions of the lesion have become anaplastic.

RECENT OBSERVATIONS IN RADIOSENSITIVITY

Regaud and Nogier[9] and also Delbet in 1918 observed that when radiation is administered by repeated exposures over a prolonged interval the tumor cells become more resistant and develop a radioimmunity, whereas the normal cells become more radiosensitive and more subject to radionecrosis. These observations have been amply confirmed by subsequent clinical observation. Regaud in 1922, Schinz and Slotopolsky in 1926 and Regaud and Ferroux[10] in 1927 demonstrated that it was impossible to cause the complete sterilization of the rabbit's testis by a single irradiation without causing serious lesions of the skin. The threshold dose for the production of radionecrosis was from 4,000 to 4,400 roentgens (Solomon) when administered in one dose and 6,200 roentgens (Solomon) when administered over a period of two weeks. At the same time the threshold of sterilization of the seminal epithelium did not increase in a parallel

9. Regaud and Nogier: Compt. rend. Acad. d. sc. **158**: 1711, 1914.
10. Regaud, C., and Ferroux, R.: Paris méd. **1**: 382 (April 26) 1930.

manner but remained in the neighborhood of 5,000 roentgens (Solomon) when the dose was administered in equal parts over a period of from four to nine days. Thus it was shown experimentally that by prolonging the time of treatment the threshold of cutaneous necrosis is increased by 50 per cent while at the same time the threshold of sterilization is maintained at its original level.

The saturation method of Pfahler in America resembles to some extent the technic of Coutard, although the underlying radiophysiologic principles differ somewhat in the two methods.

The experimental studies of Regaud, Lacassagne,[11] Nogier and Ferroux, and the clinical observations of Coutard,[12] Monod,[13] Schintz, Pfahler, Berven[14] and others have swung the pendulum from single massive doses to that of protracted and more or less continuous irradiation. The clinical results of the protracted technic in the treatment of carcinoma of the tonsil, pharynx and larynx by means of roentgen therapy recently reported by Coutard and Berven's results in carcinoma of the tonsil by teleradium therapy mark most important advances in the radiation treatment of neoplastic diseases.

According to Coutard's method the lesion is exposed to x-rays twice daily with 4 milliamperes, 200 kilovolts, 2 mm. of copper filtration, and at distances varying from 50 to 90 cm. The criterion of dosage is biologic rather than physical. Treatment is continued until there develops in the normal tissues around the lesion a condition that has been called "epithelite."

Pursuing these general principles, I have adopted a technic of teleradium therapy that differs from the Coutard method first in utilizing the more penetrating gamma rays of radium and, secondly, in extending more fully the principle of continuity of radiation. By this method the lesion is exposed to the gamma rays of radium (4 Gm. pack and 2 Gm. pack) twice daily on consecutive days without interruption for periods varying between twenty and sixty days. Treatment is continued until the characteristic reaction is observed in the normal tissues surrounding the growth. In this way it is intended to collect and record a series of observations, which it is hoped may ultimately permit a comparison between the biologic effects and clinical results of x-rays and gamma rays. There is considerable clinical evidence to suspect that continuity of radiation may be one of the most important factors in the sterilization of neoplasms by means of radiotherapy.

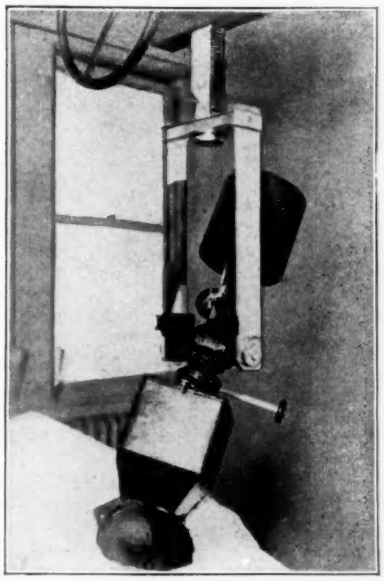

Fig. 12.—Four Gm. radium pack, showing counterweight and compartment containing 4 Gm. of radium with mercury protection.

One of the most important problems that confront physicians today is the question of the total interval during which radiation is best administered. There is a possibility that such an interval may vary for the different tumors. A determination of the optimal interval for each type of growth constitutes an important clinical and biologic research, which is under way at the present time. Another factor that remains undetermined is the question of the intensity of radiation. Thus it is not fully established whether the administration of 100 roentgens during a period of five minutes differs from the administration of a similar dose during a period of one hour. This question raises problems that are not only of great medical interest but also of considerable economic importance. Investigations bearing on these various questions at present occupy the attention of the various radiotherapeutic centers throughout the world.

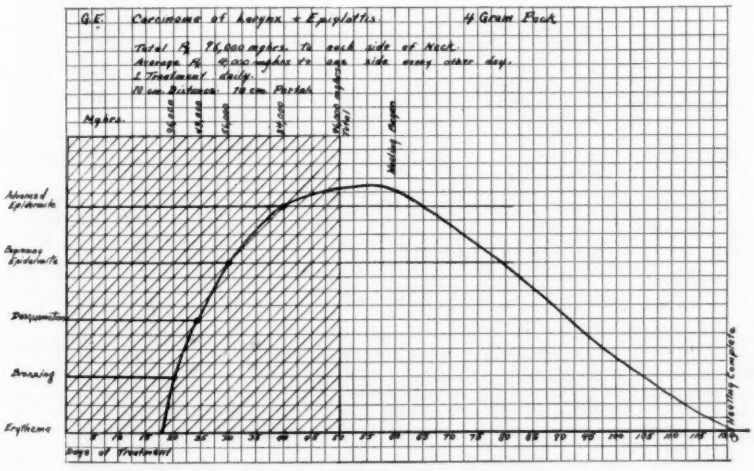

Fig. 11.—Curve showing the relation of the skin reaction following radium pack therapy to time of treatment and dosage.

ABSTRACT OF DISCUSSION

DR. JOSEPH C. BLOODGOOD, Baltimore: I think that I am rather the proper person now to discuss the treatment of malignant disease by other means than surgery. I do not think that I have changed from surgery to radiotherapeutics except by the contemplation of facts. That report at my clinic told me that 49 per cent of the patients previously operated on in the clinic now go to Dr. Burnham and Dr. Neil for radiotherapy. This is based on results. They are not inoperable; they are still operable. They are not hopeless cases; they are still hopeful, but they get well under radiotherapy. This has happened during the last three years, not because I have changed any but because the method of radiotherapy has changed. A great change has taken place. First of all, radium and x-rays are no longer looked on as a last resort. Dr. Horsley and I have lived through that phase of surgery when surgeons were looked on as a last resort. I never saw an appendix removed in Philadelphia when I was a student. I have lived through good surgery, and I am living in the time of good radiation. Frankly, the evidence that I have today suggests that the time of removing the breast for a microscopic cancer is almost over. One has to get a lump that is of one month's duration and is smaller than a twenty-

11. Lacassagne, A.: Radiophys. et radiothérapie **1**: 401, 1930.
12. Coutard, H.: Radiophys. et radiothérapie **2**: 541, 1932; Am. J. Roentgenol. **28**: 313 (Sept.) 1932.
13. Monod, O.: Radiophys. et radiothérapie **1**: 207, 1928.
14. Berven, E.: Acta radiol., supp. **11**: 1, 1931.

five cent piece (24 mm.), and one has only to find it with a microscope. The chief reason for using radiation therapy will not be that one is certain that it is cancer or not, but that one is uncertain. The majority of lumps of one month's duration and smaller than a twenty-five cent piece are going to be difficult to diagnose as cancer. I remember my reaction in the beginning to the statements of Pfahler. I did not believe a word he said, but I believe them now, because when I accumulated all the cases of jaw tumors that we had in forty years, Pfahler's name stood next to all the living patients who had irradiation. He was the beginning of Coutard's method. I have seen Coutard. I have sat next to him all day long and have seen cancer of the tonsils and of the base of the tongue after five, seven and ten years. I have seen the same thing happen in Baltimore in the hands of Dr. Burnham and Dr. Neil. In cancer of the jaw I know that I have cured 10 per cent of my cases by resecting, and the patients have lived for five years, but mighty few of them are alive after ten years. I do not believe any one has faithfully studied, as I did with Dr. Halsted, beginning first in 1895, forty years ago, the actual results of what I believe can be said today to have been the best surgery. I have seen the results abroad. I saw cancer of the rectum with two great men in London. I am now seeing radiation replace surgery, certainly in the mouth. Of course, warts, skin lesions, and lesions everywhere that can be cut out can be taken off without any mutilation, with 100 per cent results. I think those cases will still be surgical. The radiotherapist has to be just as much a pathologist as the surgeon, and I don't know but that he will have to spend less time in anatomy and more time in pathology, because a pathologic point of view will give courage and direction to all who are treating cancer.

DR. J. SHELTON HORSLEY, Richmond, Va.: I cannot go quite as far as Dr. Bloodgood in repudiating surgery in the treatment of cancer, but I think there is a decided and beneficial tendency toward using irradiation rather than surgery in certain types of malignancy, such as those Dr. Cutler has shown. In many others, a combination of intelligent radiotherapy with excision is beneficial. One must bear in mind, however, that radiation is just as dangerous as a knife. If I had to choose between being operated on by an incompetent surgeon with a sharp knife and being treated by an incompetent radiologist with a powerful x-ray machine, I think I should take my chances with the knife. The indications for the proper treatment of any malignant condition should be carefully studied in every branch of clinical medicine. It is becoming more and more necessary to hitch up pathology with all clinical treatment, for clinical treatment cannot be intelligently carried on without some knowledge of the organic pathologic changes or the perverted physiology that causes the disease.

DR. E. B. KRUMBHAAR, Philadelphia: As I recall Dr. Cutler's definition of radiosensitivity, it implied that all cells of the neoplasm could be destroyed without permanent damage to the surrounding normal tissue. I believe that that would mean a cure, for if all the cells of a neoplasm are destroyed, that particular neoplasm is cured, and even if another neoplasm occurs and occurs in the same place, that is another neoplasm. In this sense, also, the term "relatively radioresistant" is meaningless. Either the tumor can have all its cells killed, or it cannot. Furthermore, I don't believe that in Hodgkin's disease it is ever clinically possible to kill the cells of the Hodgkin's lesion. Therefore, I would not agree to calling Hodgkin's disease a radiosensitive disease in this sense.

DR. MAX CUTLER, Chicago: Since there are varying degrees of radiosensitivity, it is not possible to divide all tumors sharply into two groups. The definition of radiosensitivity is therefore an arbitrary one. The definition of radiosensitivity that I have stated in this communication is that which has been proposed by Regaud and is generally accepted by workers in this field. It is based on well established biologic principles and is practically useful for clinical purposes. In stating that certain forms of Hodgkin's disease are radiosensitive I refer to the highly cellular forms which clinically and microscopically simulate lymphosarcoma so closely that a distinction between the two processes is often not possible. I wish to thank those who have taken part in this discussion.

VALUE OF FRIEDMAN TEST IN DIAGNOSIS OF INTRA-UTERINE AND EXTRA-UTERINE PREGNANCY

MORRIS A. GOLDBERGER, M.D.
UDALL J. SALMON, M.D.
AND
ROBERT T. FRANK, M.D.
NEW YORK

In a review [1] of 4,595 Friedman tests performed by twenty-six different clinical pathologists, it was shown that 5.1 per cent of the tests were false negatives and 0.95 per cent were false positives. In ectopic pregnancy 77.8 per cent were correct positives and 22.2 per cent were incorrect negatives. The technic employed in this series consisted of the injection of 10 cc. of urine into one nonpregnant mature female rabbit followed by gross inspection of the ovaries forty-eight hours later.

At Mount Sinai Hospital, 1,137 Friedman tests have been performed to date. The technic employed differs

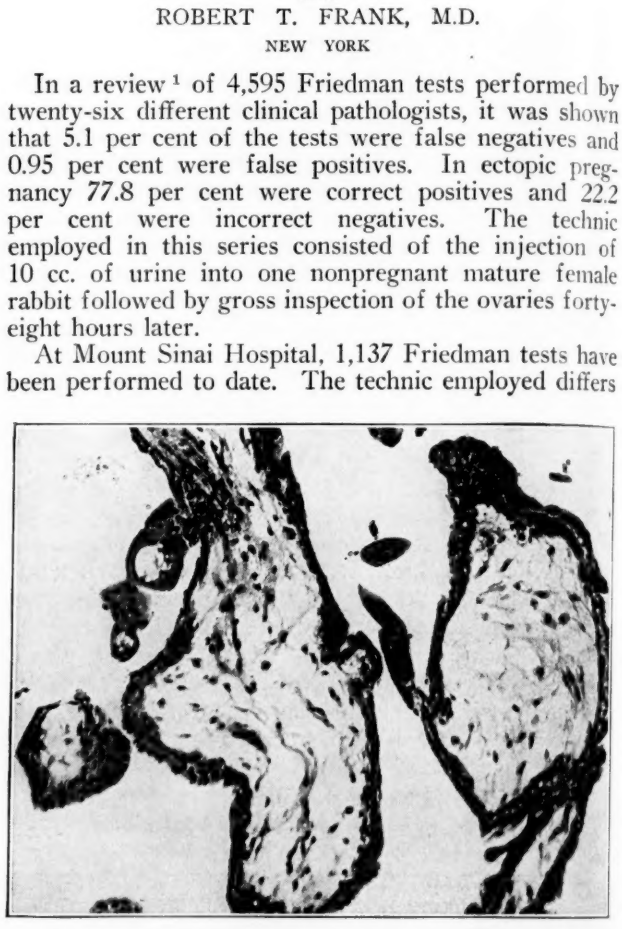

Fig. 1.—Normal chorionic villi from ectopic pregnancy. Friedman test positive. The villus stroma, Langhans cells and syncytium are well preserved.

from that reported by others in that 20 cc. of freshly voided morning urine is used and the test is done in duplicate; i. e., two mature nonpregnant female rabbits are used for each case. Five cubic centimeters of urine is injected in the morning and afternoon on two successive days and the ovaries are inspected grossly forty-eight hours after the first injection.

With the employment of this technic in 1,093 intrauterine pregnancies, there were six false negatives (0.55 per cent) and one false positive (0.09 per cent). The latter proved to be negative when repeated two days later and was found to be due to an error in labeling two specimens received on the same day. The smaller percentage of error in our series is probably attributable to the one essential point in which our technic differs from that generally employed; viz., the use of two rabbits for each test. The value of using two rabbits is demonstrated by the fact that, in twenty-two of our first 635 cases, one of the two rabbits was negative in proved cases of pregnancy. This would

From the Gynecological Service and the Division of Laboratories of the Mount Sinai Hospital.

1. The Friedman Hormone Test for Pregnancy, editorial, Am. J. Clin. Path. **3**: 97 (Jan.) 1933.

indicate that at least 3.4 per cent of rabbits are refractory to pregnancy urine.

The value of the Friedman test in ectopic pregnancy is worthy of consideration, as it is in this type of pregnancy that the diagnosis is most often in question.

In forty-four ectopic pregnancies in which Friedman tests were done in duplicate, there were fourteen false negatives (32 per cent error). In this series, the Friedman test was considered to be of value only when it was positive. Not infrequently the diagnosis of ectopic pregnancy was made from the history and clinical observations, in the face of a negative test.

The high percentage of false negatives in ectopic pregnancy can be accounted for if one studies the histologic structure of the specimens removed at operation. In every one of these specimens examined there were either degenerated or necrotic villi. In twelve instances the villi exhibited various stages of degeneration, the majority being necrotic, appearing merely as "ghosts" (figs. 1 and 2). In one instance there was a four months macerated fetus; in another, no villi were found. The latter specimen was reported by the pathologist as a "hematosalpinx, probably an old ectopic."

Of the thirty cases of ectopic pregnancies with positive Friedman tests, well preserved villi were found in the specimens of twenty-two; villi in various stages of degeneration were found in three and no villi in five.

As the positive Friedman test is dependent on the presence in the urine of the anterior pituitary-like hormone elaborated in response to activity of the chorion, it is obvious that with death or degeneration of the chorionic villi the test will become negative. Keeping in mind the fact that quite frequently when the Friedman test is done in a case of ectopic pregnancy there has already occurred either tubal abortion or rupture, so that the chorionic tissue is either degenerated, dead

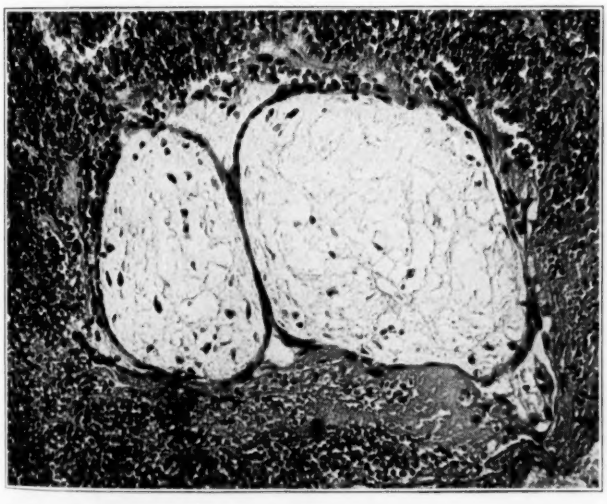

Fig. 2.—Degenerated chorionic villi from ectopic pregnancy; Friedman test negative. The villus stroma is beginning to disintegrate. The Langhans cell layer is incompletely degenerated; remnants of syncytium are still present.

or completely separated from the circulation of its host, the high percentage of false negatives becomes understandable.

How is one to account for the positive tests in the three cases with degenerated villi? As serial sections were not made, it is quite possible that there may have been some active chorionic tissue present which was overlooked. Furthermore, while judged by morphologic criteria the chorionic villi are classified as "degenerated" or "ghosts," there is no way of estimating whether or not these villi still have some activity. As regards the five cases with positive tests in which no villi were found, we are forced to the conclusion that the ovum and chorion were lost among the blood clots.

In this connection it is worth while remembering that in intra-uterine pregnancy the Friedman test will

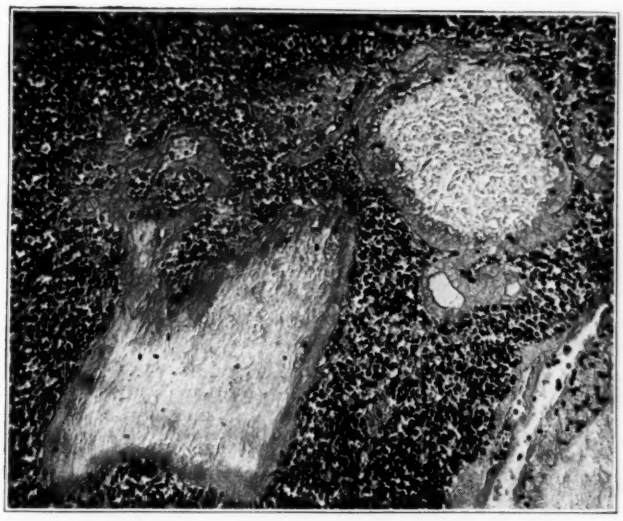

Fig. 3.—Completely degenerated chorionic villi, "ghosts of villi" from ectopic pregnancy; Friedman test negative. There is entire absence of cellular structure; the villus stroma and cellular outline are hyalinized.

become negative if there is either complete separation or degeneration of the chorion. On the other hand, with a dead fetus, as long as the chorion is preserved, the test will remain positive. We have found the Friedman test positive as long as thirty days after death of the fetus. Death of the fetus was determined by the disappearance of female sex hormone from the blood, as previously reported.[2] In another case of fetal death a positive Friedman test was obtained with as little as 0.5 cc. of urine. The curettings in this case revealed well preserved placental tissue.

The Friedman pregnancy test is a valuable laboratory aid in the diagnosis of pregnancy. Like other laboratory tests, however, it has its limitations. For the clinician, it is important to remember that a positive test means merely that the patient is excreting anterior pituitary-like hormone which is formed in response to the presence of viable chorion, that the positive test does not indicate whether the fetus is alive or dead, that the test will remain positive in missed and in incomplete abortions as long as viable chorion is attached to the uterine wall, and that a negative test does not exclude the presence of an ectopic pregnancy.

SUMMARY AND CONCLUSIONS

1. In 1,093 normal intra-uterine pregnancies the percentage of false positive Friedman tests was 0.09. The percentage of false negatives was 0.55.

2. This small percentage of error, as compared to other reports, is attributed to the fact that duplicate tests were performed.

3. At least 3.4 per cent of rabbits appear to be refractory to the Friedman test.

2. Spielman, Frank; Goldberger, M. A., Frank, R. T.: Hormone Diagnosis of Viability of Pregnancy, J. A. M. A. **101:** 266-268 (July 22) 1933.

4. In ectopic pregnancy, the percentage of false negatives in a series of forty-four cases was 32.

5. The high percentage of negative tests in ectopic pregnancy is accounted for by the presence in these cases of dead or degenerated villi.

6. In both intra-uterine and extra-uterine pregnancies the Friedman test is dependent on the viability of the chorion.

7. In missed abortion the Friedman test may remain positive for as long as thirty days after death of the fetus.

8. In incomplete abortion the Friedman test may be positive.

9. The presence of a viable fetus can be determined by study of the female sex hormone of the blood.

10. In the diagnosis of ectopic gestation the Friedman test is of value only in cases in which it is positive.

11. If the test is negative in a case of suspected ectopic pregnancy, the clinical history and observations should determine the diagnosis.

145 West Eighty-Sixth Street.

Clinical Notes, Suggestions and New Instruments

ESTRIN IN HIGH CONCENTRATION YIELDED BY A FIBRO-ADENOMA OF THE BREAST

DEAN LEWIS, M.D., AND CHARLES F. GESCHICKTER, M.D.
BALTIMORE

Diffuse and localized hypertrophy of the breast occurs relatively frequently in both the male and the female. In gynecomastia the hypertrophy may be unilateral or bilateral, but it is usually diffuse. The unilateral type is the more common. The localized change (the so-called fibro-adenoma) is the most common form in the female breast. Diffuse hypertrophy of one or both breasts, known as virginal hypertrophy, is most frequently bilateral. Gynecomastia, fibro-adenoma, and virginal hypertrophy are in almost all instances benign. In extremely rare instances a fibrosarcoma is supposed to have developed in or from a preexisting clinically benign fibro-adenoma.

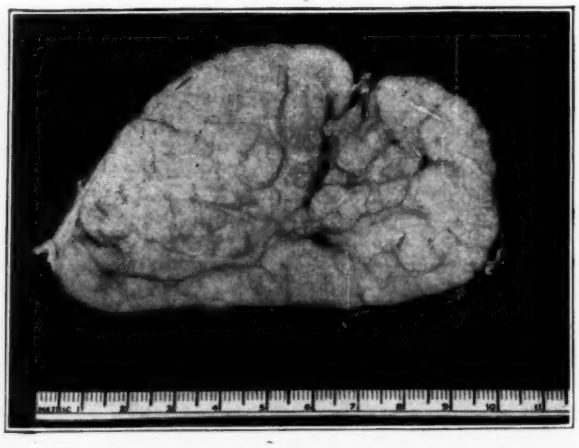

Fig. 1.—Fibro-adenoma occurring in a Negro girl aged 12 years. Menstruation was not established. This shows a section from the mid-section of the gross specimen. The remainder of the specimen was ground and assayed for estrin and showed a concentration in excess of 5 rat units per gram of tissue.

Histologically these benign lesions are characterized by an increase in the length and diameter of the ducts, an increase in the number of layers of epithelium lining the ducts, and a proliferation of the periductal connective tissue. The histologic picture is essentially an exaggeration of that observed in the normal female breast when puberty hypertrophy is taking place.

In the adolescent girl, normally, definite changes begin from three to five years before menstruation is established. Enough clinical and experimental evidence has accumulated to warrant one in assuming that there is a direct relationship between ovarian hormones and the changes occurring at puberty. Having such a relationship in mind, we desired to determine whether estrin could be found in such tumors and, if so, in what amounts. Our observations were so striking that we feel justified in recording the following case:

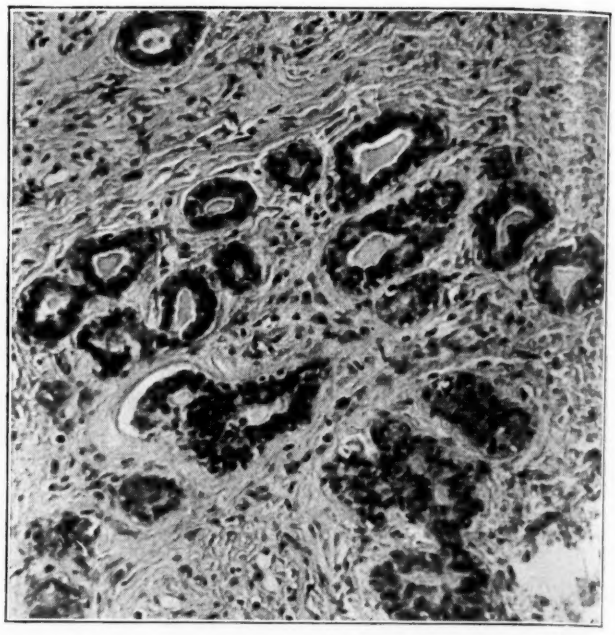

Fig. 2.—An area from the specimen shown in figure 1 showing a typical fibro-adenomatous appearance.

A Negro girl, aged 12 years, had had no previous illness, with the exception of recurrent attacks of tonsillitis and chickenpox at 5 years. She weighed 105 pounds (47.6 Kg.). Two years before admission to the hospital the breasts began to enlarge. The enlargement apparently proceeded normally, although the patient's mother said that she thought the breasts were unequal in size. Sometime before admission to the hospital, however, a distinct mass, which grew rapidly, was found in the left breast. This mass was not tender, and attention was attracted to it because of the size.

The girl was well developed. She had a slight scoliosis. The right breast was definitely larger than the breast of a girl of the same age normally would be. The left breast was almost twice as large as the right. It contained a nodular mass about the size of a medium size adult fist. The mass was freely movable, being attached neither to the skin nor to the underlying structures. The skin over the tumor was normal. No abnormalities of the nipple were noted. There was no discharge from the nipples.

April 23, 1934, the tumor in the left breast was removed with some of the overlying skin. Microscopically this tumor was a typical fibro-adenoma. The breast tissue surrounding the tumor showed an increase in the number and size of milk ducts and an increase in the periductal connective tissue.

The tumor, with the exception of a small section saved for microscopic examination, was placed in 95 per cent alcohol. This was sent to Dr. J. A. Morrell of the Biological Laboratories of E. R. Squibb and Sons, through whose kindness the tumor was assayed for estrin. Dr. Morrell makes the following statement concerning the assay: "The tissue contains a great deal more estrin than I had anticipated. It looks as though it contains more than 5 rat units per gram of tissue.

Aided by a grant from the Anna Fuller Fund.
From the Department of Surgery (Surgical Pathological Laboratory), Johns Hopkins Hospital and University.

You will agree with me that this is rather remarkable when we find that the maximum which we can obtain from the hog's ovaries by an identical extraction procedure is about 50-75 units per pound of ovary. In other words, hogs' ovaries contain approximately one unit to every 9 Gm. of tissue, so that your breast tumor contains more than forty-five times as much estrin per unit weight." [1]

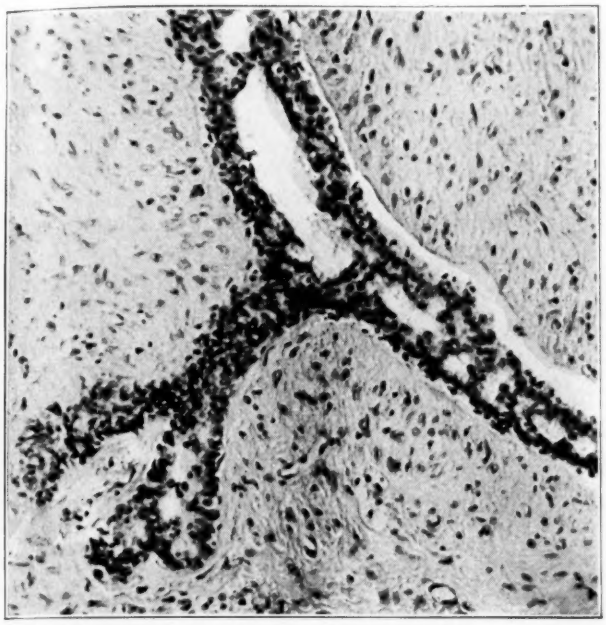

Fig. 3.—Another area of the specimen shown in figure 1. The connective tissue in the tumor is compressing the ducts, which have undergone a marked hypertrophy.

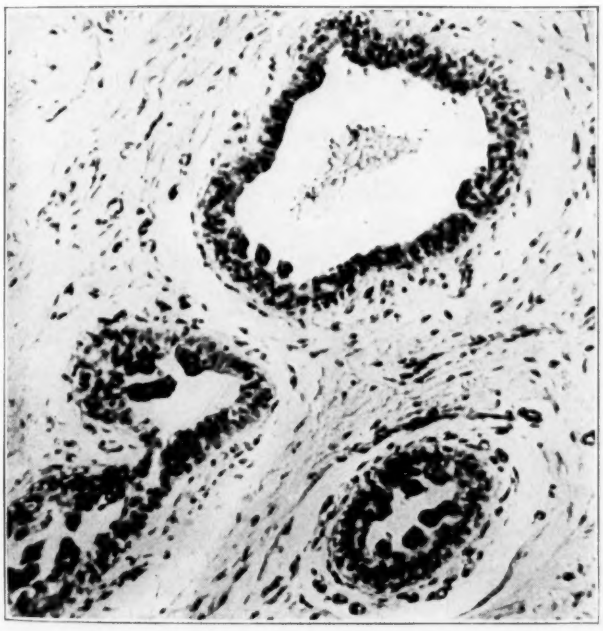

Fig. 4.—Appearance under high power of the breast tissue surrounding the tumor shown in figure 1. The increased number of cell layers in the duct lining and the increase in periductal connective tissue in the tissue surrounding the tumor is possibly in response to a higher level of estrin in the blood.

Hypertrophy of the breast may be produced experimentally in both male and female monkeys by injections of estrin. Large quantities of estrin were found in the tumor just described. We believe that such an abnormal concentration may have an etiologic significance in the production of such a growth.

1. The final bio-assay showed 6 rat units per gram of tissue, or nearly 3,000 rat units per pound.

Special Articles

THE PATHOLOGY OF AMEBIASIS

CLINICAL LECTURE AT CLEVELAND SESSION

HENRY E. MELENEY, M.D.
NASHVILLE, TENN.

The papers by Drs. Meleney, Magath and Reed in this issue complete the series of clinical lectures on amebiasis read at the Cleveland session. The papers by Drs. Craig and Simon were published October 6, and the papers by Drs. McCoy and Chesley and by Dr. Lynch were published October 13.

Any description of the pathology of amebiasis must pay tribute to Councilman and Lafleur,[1] who in 1891 first described the lesions in detail and differentiated them from the lesions of bacillary dysentery, and to Leonard Rogers,[2] Kartulis,[3] Kuenen,[4] Craig,[5] James [6] and many others who have made contributions to the subject since that time.

The action of Endamoeba histolytica is fundamentally the same in all the tissues that it invades and in all susceptible animals into the tissues of which it gains entrance. This action is based on two weapons of

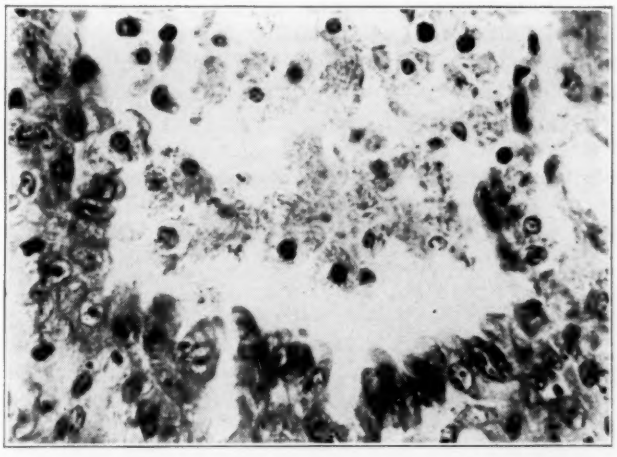

Fig. 1.—Earliest amebic lesion of the colon. A depression in the mucosa showing amebas in the lumen and beginning to invade and destroy the epithelium. One ameba is seen penetrating between two epithelial cells at the left, and another lies beneath several degenerated epithelial cells at the right. Kitten specimen. The amebas can be identified by their nuclei, which have a heavy ring of peripheral chromatin and a small central karyosome (nucleolus).

attack possessed by the ameba; namely, mechanical invasion by means of pseudopods and a toxin that acts directly on the tissues of the host. With these facts in mind it is possible to trace the development of amebic lesions wherever they occur and to understand the fully developed picture that is usually seen in man.

From the Department of Preventive Medicine and Public Health, Vanderbilt University School of Medicine.

Read in the General Scientific Meeting at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 12, 1934.

The author is indebted to the Department of Pathology of the Vanderbilt University School of Medicine for preparing the photomicrographs accompanying this paper, and to that department and the Departments of Pathology and Surgery of Columbia University College of Physicians and Surgeons for sections of tissue from which some of the photomicrographs were made.

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AMEBIC LESIONS OF THE INTESTINE

In the first attack on the wall of the intestine, amebas are sometimes found on the surface of the mucosa in contact with epithelial cells, which show obvious toxic damage (fig. 1), or they may first be found beneath the epithelium with no apparent break in the epithelium.

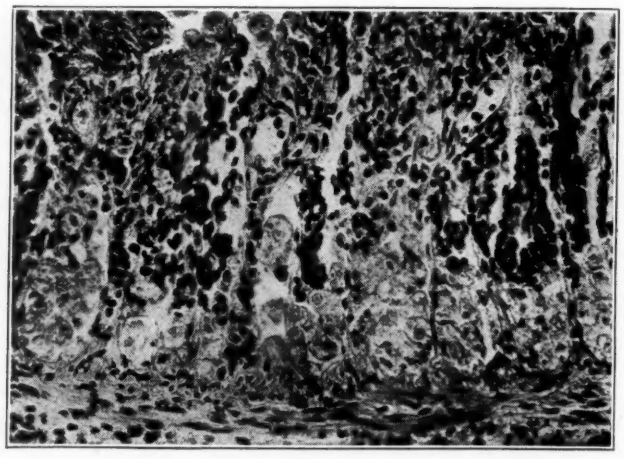

Fig. 2.—Amebas congregated beneath the epithelium in the fundi of vertical glands of the colon. Kitten specimen.

This first attack may occur in a depression between rugae or in the lumen of a vertical gland, or it may occur on the surface epithelium between glands.

Having penetrated the epithelium, the amebas either advance along the basement membrane to the fundi of the intestinal glands, where they congregate and multiply (fig. 2), or they may penetrate the basement membrane near the surface of the mucosa and enter the connective tissue stroma between the glands. Here they pass down toward the muscularis mucosae, causing edema and necrosis of the tissue and dilatation, rupture or thrombosis of capillaries. Ultimately the necrosis involves the entire thickness of the mucosa. It may extend laterally over a wide area, or it may be sharply limited to a small group of glands.

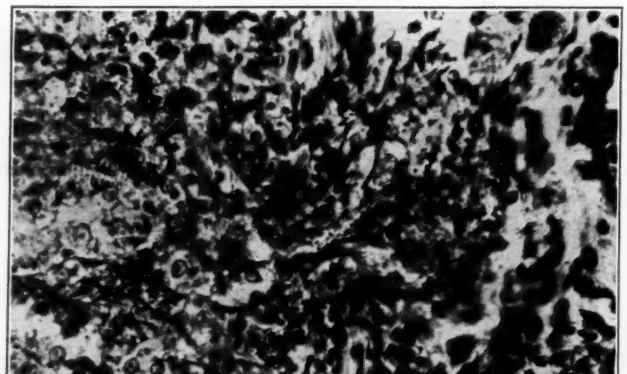

Fig. 3.—Amebas in a lymph vessel leading through the muscularis mucosae into the submucosa of the colon. Kitten specimen.

The amebas in the fundi of the glands soon break through the basement membrane and join those from the stroma of the mucosa in penetrating the muscularis mucosae either through tissue spaces or in the lymph or blood vessels (fig. 3).

In the submucosa the amebas spread out in all directions between the connective tissue fibers. Their toxin causes edema, fibrin formation and degeneration of cells and intercellular fibers. The submucosa often becomes several times its normal thickness. There is little or no cellular response on the part of the host, so that few polymorphonuclear leukocytes and only moderate numbers of mononuclear cells may be found in the lesions; but when bacteria gain access to the tissues, especially gram-positive cocci, there is a marked polymorphonuclear response and the degenerating submucosal lesion takes on the appearance of a pyogenic abscess with few amebas in it. At the periphery of such a lesion, bacteria are usually absent, but numerous amebas are present in the advancing area of edema and necrosis (fig. 4).

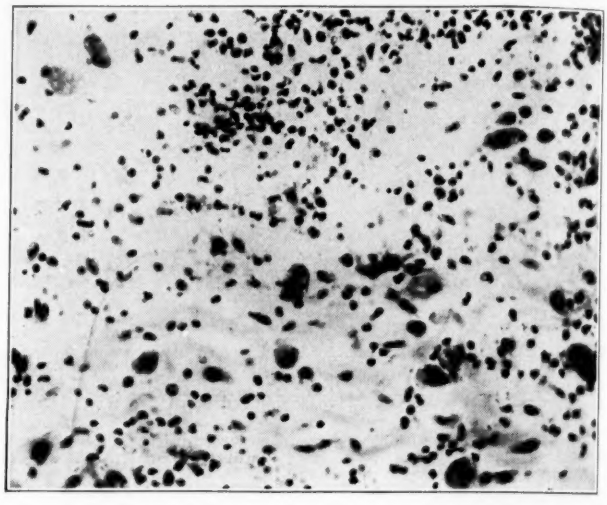

Fig. 4.—Amebas in the edematous submucosa at the margin of an ulcer. Human case.

Meanwhile if the lymphatics of the mucosa have been opened by necrosis, those of the submucosa may become filled with necrotic cells and bacteria, together with amebas that have entered them in the mucosa. This is more strikingly seen in kittens than in man (fig. 5). In the submucosa the amebas also attack the walls of lymph and blood vessels and are often found in their lumens. Thrombosis of the blood vessels thus attacked is commonly seen.

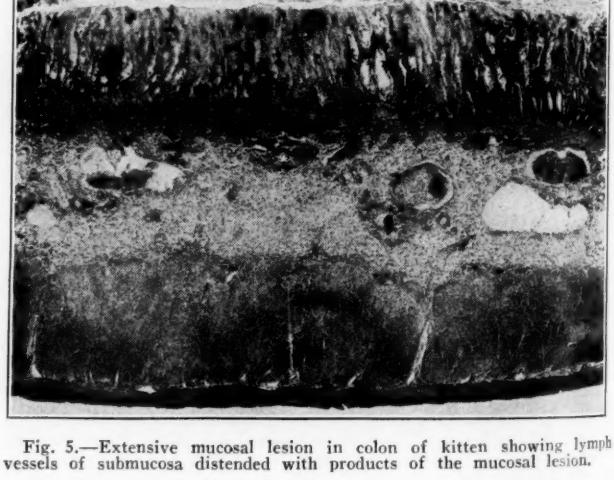

Fig. 5.—Extensive mucosal lesion in colon of kitten showing lymph vessels of submucosa distended with products of the mucosal lesion.

Although amebas enter the lymph vessels and are undoubtedly carried in them to the mesenteric lymph nodes in many cases, amebic lesions in lymph nodes are practically unknown either in experimental animals or in man.

The lateral extension of the lesions in the submucosa leads to the cutting off of the circulation in the mucosa over the necrotic area. At the same time the discharge of the contents of the submucosal abscess allows the edges of the mucosa to collapse into the cavity thus formed. As the mucosa disintegrates the opening becomes larger, until an ulcer of considerable size may be developed (fig. 6). Frequently adjacent submucosal lesions coalesce, leaving a bridge of normal mucosa over a communicating channel underneath.

The muscular coats of the intestine offer a temporary barrier to the amebas, but the connective tissue septums between muscle bundles furnish paths along which the amebas reach the outer muscular coat and the subserous tissue (fig. 7). Gradually they also penetrate the muscle cells and cause edema, hyalinization and finally necrosis of this tissue. Secondary invasion by bacteria assists in the extension of the ulcer into this layer of the wall.

In the subserous tissue the amebas produce edema followed by the formation of fibrin on the serous surface, which leads to adhesions of apposing peritoneal surfaces. If the necrotic process penetrates through the muscle layers, the serosa easily gives way and perforation occurs.

Fig. 6.—Section of human colon showing two deep submucosal lesions with overhanging margins of mucosa. Note thickness (edema) of submucosa and puslike contents of the ulcers.

The lymph follicles of the colon play a minor rôle in the amebic lesions in man. They may, however, be invaded either directly from the surface or by amebas advancing in the submucosa, and they may become involved in the abscess-like lesions by direct extension. The amebas that enter lymph follicles from the mucosal surface advance radially toward the periphery of the follicles, and necrosis and secondary bacterial invasion follow.

The process that has been described represents the unobstructed development of the severest type of amebic lesion in the colon. Sometimes, however, in persons dying of other diseases, although no gross amebic lesions are visible at autopsy, microscopic lesions are found in tissue sections. In such lesions there may be no definite necrosis of the tissues. The glandular epithelium is usually missing in small areas, but except for the presence of amebas there is very little change in the tissues (fig. 7). Such a condition probably represents either the presence of a strain of ameba of a low degree of pathogenicity or great resistance on the part of the host. It may be the condition that exists in some of the cases of amebiasis that present no clinical symptoms.

With the microscopic pathology in mind, one easily understands the gross lesions as seen on proctoscopic examination or at autopsy. The earliest lesion consists merely of a slightly raised bright red spot of hemorrhage or hyperemia. Following this there are three main types of early lesions. The first is a shallow ulceration of the mucosa surrounded by a narrow ring of hyperemia. The second is a diffuse granular appearance of the mucosa representing many points of invasion of the amebas into the glands without visible ulceration. The third and much the most common in man is a sharply circumscribed nodular projection of the mucosa with a small depressed yellow opening in the center surrounded by a hyperemic ring and leading into a cavity containing gelatinous material. This represents the early stage of the abscess-like lesions in the submucosa.

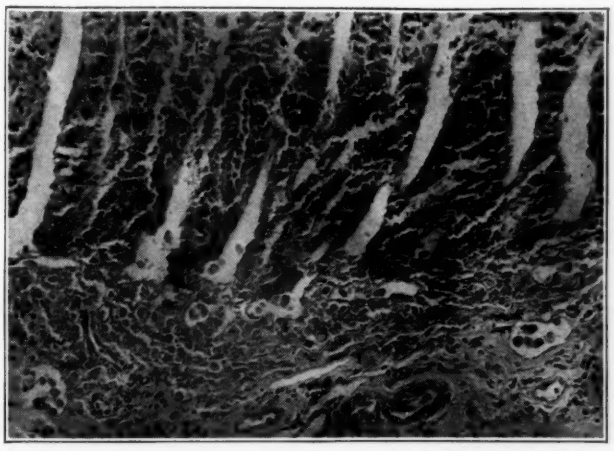

Fig. 7.—Mild amebic lesion of human colon. No gross ulcers were visible at autopsy. The glandular epithelium has disappeared and there is beginning disintegration of the connective tissue stroma of the mucosa, but not complete necrosis. Very slight edema of submucosa, where numerous amebas are present in the tissue and lymph vessels.

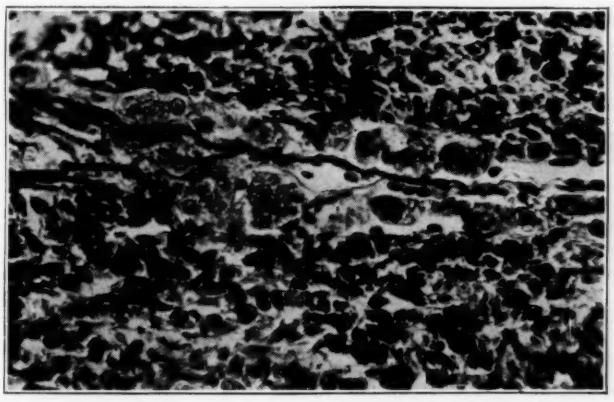

Fig. 8.—Amebas advancing in connective tissue septum between bundles of internal muscular layer of human colon. Muscle coat formed base of ulcer.

The larger ulcers vary greatly in size, shape and depth. When discrete, they often occupy the tops of rugae and extend transversely across the intestine. Their edges are raised and overhanging and the base consists of mucoid material covering the necrotic sub-

mucosa or the muscular coat of the intestine. Sloughing shreds of tissue may be loosely attached to the base of the ulcer. These ulcers often coalesce, forming large irregular areas sometimes bridged over with strands of partly necrotic mucosa. They may become very extensive, involving the entire circumference of the intestine and reaching a length of 6 inches or more. As they become deeper the inner muscular layer may be partly

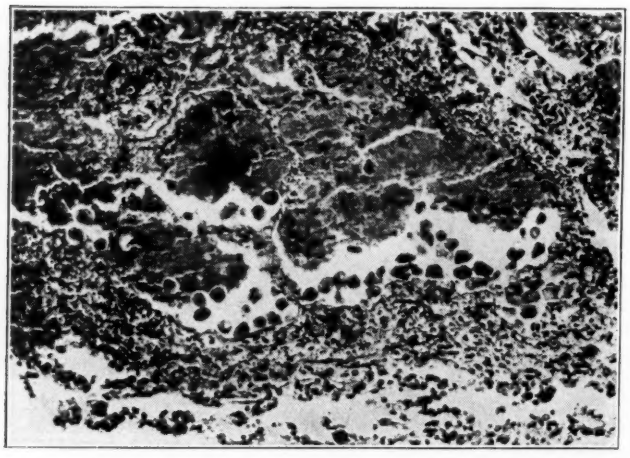

Fig. 9.—Amebic abscess of human lung with pneumonia. Note the noncellular character of the exudate in the alveoli and the absence of alveolar architecture in the abscessed portion. Many amebas distributed irregularly throughout the lesion.

separated and hang in shreds from the necrotic base. Sloughing portions of the wall may be passed out with the stools. With destruction of the circulation or invasion of the serosa, a gangrenous condition develops leading to perforation of the wall. Such perforations are often several centimeters in diameter.

Where extensive ulceration occurs there is usually a general thickening of the wall of the colon due to

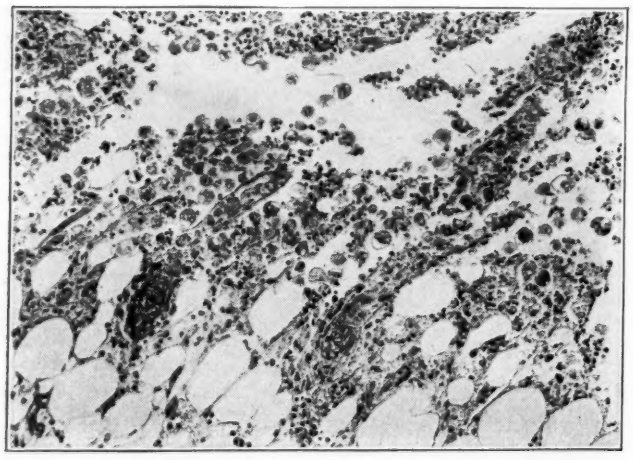

Fig. 10.—Amebic ulcer of the skin, showing invasion of subcutaneous fat by amebas at margin of ulcer.

edema, which is most marked in the submucosa; but if the lesions are discrete the appearance of the intestine between them may be normal.

Healing of intestinal lesions, if they have not advanced beyond the submucosa, frequently occurs. Lesions involving only the mucosa may leave no scar. Deeper lesions often lead to permanent thickening and rigidity or stenosis of the intestine. Peritoneal adhesions may lead to permanent functional disturbances or to kinking and obstruction. Healing and active ulceration in different parts of the same ulcer frequently are in progress at the same time.

The distribution of amebic lesions in the colon may be general or localized. Localized lesions are found most frequently in places where stasis normally occurs. In their order of frequency these places are the cecum, the ascending colon, the rectum, the sigmoid, the appendix and the splenic and hepatic flexures.[7] In general the most severe lesions tend to occur in the cecum but may be found as low as the sigmoid. Rectal ulcers are more often shallow.

In addition to the colon, the terminal portion of the ileum is occasionally found to be involved. It is probable that such involvement is always secondary to lesions in the colon.

AMEBIC LESIONS OF THE LIVER

The second great site of pathologic lesions in amebiasis is the liver. Amebas are undoubtedly transported to the liver from intestinal lesions by the portal blood stream. Councilman and Lafleur [1] and Rogers [2]

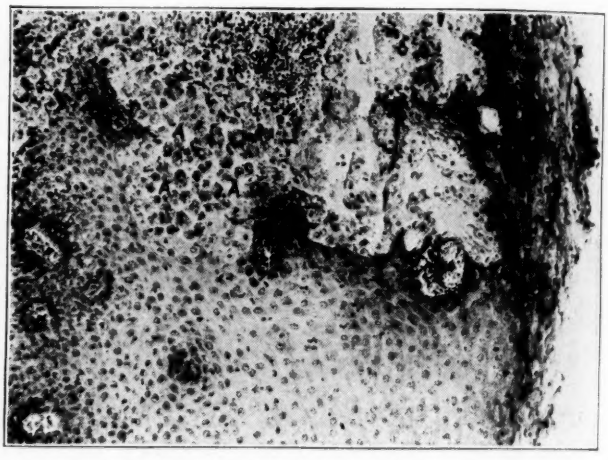

Fig. 11.—Amebic ulcer of the skin, showing amebas attacking exposed edge of epidermis.

advanced the theory that they might also reach the surface of the liver by way of the peritoneal cavity and that this was the best explanation of the frequency of single abscesses located near the surface of the liver. Such localization, however, may be due to the fact that the portal blood stream probably takes a more direct course toward the capillaries near the liver surface and thus tends to carry the amebas to such locations.

Clinically a condition termed amebic hepatitis is well recognized. This probably represents the existence of many small lesions containing amebas with the first stage of abscess formation. Such cases are usually treated with emetine and go on to recovery, which tends to confirm the diagnosis of amebic hepatitis but does not afford an opportunity to study the pathology of the condition.

The amebic liver abscess is usually single and situated in the right lobe, but there may be multiple abscesses scattered throughout the liver. If the abscesses are multiple they give rise to clinical symptoms early and are diagnosed before they reach a large size, but if

7. Clark, H. C.: Am. J. Trop. Med. 5: 157-171 (March) 1925.

the abscess is single it may reach a very large size before the diagnosis is made.

The smallest abscesses on section may be only a few millimeters in diameter. They are solid and white and still show some semblance of liver structure. In slightly larger ones the contents are gelatinous and yellow, and still larger ones contain a reddish brown fluid and shreds of necrotic tissue. In large acute abscesses the wall is usually ragged with no evidence of a fibrous capsule. In abscesses of long standing there may be a definite fibrous capsule. If secondary bacterial infection of the abscess has occurred, the contents are purulent.

Microscopically the picture is one of progressive necrosis of the parenchymatous cells of the liver, followed by dissolution of the connective tissue framework. The process extends radially as the amebas advance, always leaving a zone of collapsed stroma between the normal liver tissue and the completely necrotic center. Thrombosis of blood vessels at the periphery also occurs and may be a factor in the extension of the abscess, particularly toward the surface of the liver.[4] The absence of a cellular reaction precludes the formation of pus, while the leaking of blood from exposed capillaries probably contributes largely to the reddish color of the fluid contents of the abscess. Amebas may be entirely absent from the fluid contents of a large abscess but are numerous in the wall.

A generalized central necrosis of liver lobules was described by Councilman and Lafleur, and a portal cirrhosis is sometimes found associated with amebic abscess of the liver; but it has not been determined that either of these processes is directly related to the amebic infection.

Because of the superficial localization of the liver abscess its extension to the surface of the liver is the rule, and adhesion to the adjacent viscera or parietal peritoneum is common, often resulting in perforation or direct extension outside the liver.

AMEBIC LESIONS OF THE LUNG

The third most frequent localization of amebic lesions is in the lung. Such lesions are sometimes embolic in origin but are usually caused by direct extension of liver abscesses through the diaphragm. The abscess may rupture into the pleural or pericardial cavity, but more often the lung becomes adherent to the diaphragm and extension occurs directly into the lower lobe. The right lung is usually the one involved. With the advance of the amebas into the lung, a localized pneumonia develops with rapid formation of an abscess. Such an abscess contains the mucoid or gelatinous material that is typical of amebic lesions, together with red blood cells, amebas, large mononuclear cells from the walls of the alveoli and fragments of the elastic tissue of the lung. At the periphery of the abscess is a pneumonic process, partly interstitial in type but mainly showing the alveoli filled with fibrin and amorphous material containing very few cells. Numerous amebas are irregularly distributed in the alveoli and to a less extent in the interstitial tissue (fig. 8).

The lung abscess usually opens into a large bronchus, discharging in the sputum a brownish mucoid material containing blood and amebas. If there is a direct connection with the liver, the discharge is similar to that of a liver abscess.

AMEBIC ULCERS OF THE SKIN

The fourth most frequent site of amebic lesions is in the skin and subcutaneous tissues. Such lesions may occur after the surgical drainage of an amebic abscess, after the drainage of a ruptured appendix or ruptured ulcer of the colon, from a colostomy opening or from direct extension of rectal ulcers through the anus by way of a fistula. They would probably never occur if the primary condition was recognized as amebic and drug treatment instituted.

Amebic infection of the skin usually appears about a week after surgical drainage has been performed. It is manifested by a rapidly spreading, intensely painful ulceration in which the advance is most rapid in the subcutaneous tissue leaving overhanging edges of dying skin, outside of which is a zone of erythema. The ulcer has a necrotic base covered with sloughs. Pus can be expressed from beneath the overhanging margin. Microscopically there is edema at the margin of the lesion into which amebas are frequently seen advancing in a frontal attack. Just behind them the tissue becomes necrotic, and still nearer the open ulcer colonies of bacteria are present. The amebas invade fat tissue (fig. 9) and can sometimes be seen attacking the exposed edge of the epidermis (fig. 10). In one case complicated by diabetes[8] they were found at autopsy even within the striated muscle cells of the abdominal wall. These ulcers are always contaminated by bacteria, usually streptococci and staphylococci, which contribute to the gross appearance of the ulcers. Infiltration of polymorphonuclear leukocytes into these lesions is usually greater than is seen in lesions elsewhere in the body. Amebas are also found in the pus that can be pressed out from beneath the overhanging margin of the ulcer. Amebic ulcers of the skin are so similar in appearance to ulcers produced by bacteria alone that they should be diagnosed as amebic only by the finding of actively motile amebas containing red blood cells, and by the finding of typical vegetative forms of Endamoeba histolytica in biopsy sections.

OTHER AMEBIC LESIONS

Amebic abscesses of the brain have been reported, usually secondary to liver and lung abscesses. Amebic infections of the gallbladder and of the urinary bladder have been described, but there is much dispute about their authenticity. Hodgkin's disease and a certain type of chronic arthritis have also been described as forms of amebic infection, but these observations have not been corroborated and it may be stated with some degree of confidence that Endamoeba histolytica plays no etiologic rôle in connection with these diseases.

There are still certain questions to be answered in connection with the pathology of amebiasis. The reasons for the variability in the intensity of the lesions, the exact nature of the toxin secreted by the ameba, the possible effect of the toxin on organs other than those immediately involved, and the factors that lead to the development of liver abscesses are some of the problems that might well claim the attention of those interested in this important disease.

SUMMARY

The pathologic lesions produced by Endamoeba histolytica are the result of its mechanical invasion and

8. Engman, M. F., Jr., and Meleney, H. E.: Amebiasis Cutis, Arch. Dermat. & Syph. 24: 1-21 (July) 1931.

its toxic action on the tissues of the host. The toxic action is manifested by edema, fibrin formation, necrosis and dissolution, in varying degree according to the type of tissue involved. In the colon the mucosa is first attacked but the submucosa suffers most severely, and lesions may involve the deeper coats of the wall and result in perforation. There is very little cellular reaction unless bacteria invade the lesions. Occasionally very mild lesions are found in which amebas have invaded the mucosa and submucosa without producing definite necrosis. Partial or complete healing often takes place, and scar formation may lead to serious functional disturbances.

Liver abscess secondary to intestinal lesions is a common complication. Sometimes these abscesses are small and multiple, but more often they are large and single and situated in the right lobe. Extension of liver abscesses through the diaphragm into the lung is common, with development of a secondary lung abscess surrounded by pneumonia. Extension into the pleural and pericardial cavities also occurs.

Amebic lesions of the intestine or liver may also extend by direct contact into other adjacent organs or tissues. Amebic ulceration of the skin occasionally occurs following the drainage of visceral lesions or by direct extension through the anus from rectal ulcers. Amebic abscess of the brain is a rare though well recognized condition. The amebic etiology of other clinical conditions has not been established.

THE LABORATORY DIAGNOSIS OF AMEBIASIS

CLINICAL LECTURE AT CLEVELAND SESSION

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ROCHESTER, MINN.

It has been generally agreed by experts in the subject that the absolute diagnosis of amebiasis is accomplished only when Endamoeba histolytica has been identified in the stool, tissues or bodily discharges. To do this clearly requires a special knowledge of protozoa in general and specific knowledge of parasitic forms. Medical schools do not as a rule train physicians to diagnose these species, and only those having special training and experience are competent to make such diagnoses.

It is my purpose in this paper to outline briefly the general phases of the laboratory diagnosis of amebiasis so that the outline may serve as a general, practical guide to the subject, and to summarize the present status of various forms of examinations.

It is obvious that the most direct method of diagnosing amebiasis is finding the parasite in the stool. If the diagnosis is for the purpose of a survey and large numbers of persons are to be examined, one will of necessity proceed along slightly different lines than if the diagnosis concerns an individual presumably suffering with symptoms of the disease. Except under rare circumstances, for purposes of a survey it will be best to examine natural fecal specimens and not those resulting from the administration of a laxative or cathartic. Usually it will be necessary for the individual to bring the specimen to the laboratory, as facilities rarely can be provided to accommodate large numbers of persons at a convenient time. The stool should be well formed, for loose or watery stools are not suitable for such surveys unless facilities are at hand for collecting the stool at the place of examination.

The most practical container is a pasteboard, paraffined, half-pint carton; on the top should be clearly marked the person's name and address, and the date the stool was passed. If medicolegal or official matters are involved, the container should bear identifying marks, and the conditions for the passage of the stool must be such that a responsible person can vouch for the fact that the specimen belonged to the person in question.

The specimen should reach the laboratory as promptly as possible, but it is not necessary for it to be kept warm. A stale, dried or moldy specimen is unsuitable, but one forty-eight hours old is usually satisfactory if it has been kept reasonably cool; under favorable conditions a longer time may be permitted to elapse. However, the sooner after passage the examination is made, the better the results.

If the purpose of the examination of a stool is to diagnose amebiasis among persons suspected of suffering from the infection, it is best to collect the specimen near the laboratory. The ideal arrangement is to have the toilet facilities immediately adjacent to the laboratory. The most suitable container in which to collect the specimens is an ordinary porcelain chamber. Either formed or loose stools are suitable, depending on the subsequent method of handling the material and on certain other conditions to be discussed later. Urine should not be passed into the chamber.

If a patient is suffering from diarrhea, the stool probably will be unformed, but if it is not, and a liquid stool is desired, it is best to administer from 1 to 1½ ounces (30 to 50 Gm.) of magnesium sulphate. This should be given about 7 a. m. and the patient instructed to eat his normal breakfast and to report to the laboratory about 8 o'clock. Usually the specimen will be passed before 10 o'clock. If the bowels are constipated, the patient should take an enema the evening before and, if the first stool after the salts is not soft, the next specimen should be examined.

Under no condition should any but a saline or nonoily cathartic be used, and oily preparations should be avoided for at least forty-eight hours preceding the test. Barium mixtures for purposes of taking roentgenograms should be avoided for at least seventy-two hours preceding the test.

If the stool is unformed, it should be examined as soon after passage as possible, preferably at once. If some delay must occur, the stool should be kept at body temperature. In no event should more than a few hours elapse before examination and, if facilities for keeping the stool warm are lacking, the examination must be made at once.

In dealing with hospital patients it requires the closest cooperation between the nursing staff and the laboratory personnel to obtain fresh, warm stools for examination and, if specimens have to be transported to other buildings, the most satisfactory method is to place the vessel containing the specimen in a specially constructed, warm, padded box. Under certain conditions it is advisable and preferable for the examiner to take his microscope to the bedside. Too much atten-

From the Section on Clinical Pathology, the Mayo Clinic.
Read before the General Scientific Meeting at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 12, 1934.

tion [redacted]ven to this phase of the work, for, if accurate [redacted]s are to be made on loose stools, the specimen must be fresh and kept warm until the portion to be examined is placed on the slide.

It is evident from the foregoing that it is not practical to examine any but formed stools sent in by mail and, if formed stools are sent by mail, the delay must be minimal.

The number of stools it is necessary to examine in order to detect parasitic protozoa has received much attention. It must be realized that in formed stools certain parasites will rarely or never be seen, as, for example, Trichomonas hominis, Dientamoeba fragilis and Balantidium coli. Hence, a protozoologic examination will not be complete unless loose stools are examined. In general, it may be said that in the formed stool cysts will be found, and that in loose stools, trophozoites, although occasionally both forms are present especially in a loose stool. As a general rule trophozoites are more difficult to identify than cysts and, unless the stools are very fresh, serious errors will result in identifying trophozoites. There is a profound difference in the demonstrability of protozoa in formed and in loose stools. From a considerable number of observations by Dobell,[1] and by Carter, Mackinnon, Matthews and Smith[2] and others, Dobell concluded that, if a large series of patients is examined, a single formed stool from each will reveal about a third of the infestations present in the series and, further, that a minimum of six such specimens from a given patient must be negative before it can be concluded that he is not infested with Endamoeba histolytica. Svensson and Linders,[3] in an elaborate mathematical treatment of the subject, concluded that about ten formed specimens are necessary in order to find all or nearly all of the infestations with protozoa, and then those which do not encyst will be missed. Examination of three stools per patient will disclose about 75 per cent of the infestations in a series.

Loose stools and those following a cathartic yield very different results. Under the conditions employed by Svensson and Linders, examination of a single specimen per patient yielded about 75 per cent of the infestations due to Endamoeba histolytica and a correspondingly high percentage of other protozoal infestations in a series.

My own observations, conducted over a period of fifteen years and resulting from more than 60,000 examinations, indicate that under proper conditions in about 80 per cent of cases, infestations with Endamoeba histolytica can be detected on the first examination, that in 95 per cent the infestation can found by examining two specimens, and that in approximately all the infestation can be detected by three such examinations.

It is obvious that a given number of stools rendered loose by catharsis will yield a higher number of positive results than an equal number of formed stools, yet the reason is by no means clear. A stool that is semiliquid or liquid is more thoroughly mixed than a formed stool and hence the loose stool offers an opportunity to obtain a better sample. However, over and above this is the clear evidence that more individual organisms are present in the loose stool than in the formed one. There are those who deny the excystation of amebas in the bowel and claim that the greater number in the loose stool is due to the sweeping out of the trophozoites by increased peristaltic action. Such an explanation is not sufficient unless one supposes that little or no division takes place normally among the trophozoites in the bowel and that the increase of water in the bowel stimulates amitotic division, since one trophozoite gives rise to only one cyst. The most logical explanation appears to be that increased moisture due to catharsis or looseness causes excystation and, hence, the increased number of trophozoites in the loose stool as compared to the number of cysts in formed stools.

It is advisable to have the entire stool from which to make preparations for microscopic examination. If the stool is formed, material should be taken from the outside as well as from the inside and, if patches of mucus, pus or blood occur, samples of these should be examined. In liquid or loose stools, material from several portions should be selected, and mucous flakes or bloody portions should be carefully noted and materials taken from such portions. In cases of amebic carriers, no special gross changes may be evident but, in acute cases, the typical stool will have dark brown streaks of mucus; the stool will be dark brick or reddish brown owing to partly decomposed blood. Sometimes flecks of bloody mucus are present, and in these flecks amebas are most numerous. Charcot-Leyden crystals are frequently present in amebic infestations, but their presence is not necessarily proof that the patient has amebiasis. In amebic stools, as a rule, there is more blood than pus and, when the reverse is true, one should think of tuberculosis or of chronic ulcerative colitis.

EXAMINATION BY DIRECT SMEAR

Microscopic preparations are made by emulsifying a small portion of the stool in a drop of saline solution placed on a clean glass slide; a coverglass is then placed over it. A dilute solution (1:1,000) of water-soluble eosin instead of saline solution may be used. This has the advantage that live amebas and other protozoa remain unstained while all other material, except fresh pus, yeast organisms and erythrocytes, is stained a pale pink, thus making a good contrast for the protozoa. A good rule to follow is to add enough stool to the diluent so that, when the coverglass is applied, one can just read news print through the slide. The emulsion should be homogeneous, and it is better to have the film too thin than too thick. Svensson and Linders recently have reported excellent results with Quensel stain, for trophic amebas, which is applied directly to the fresh preparation. A warm stage is not necessary, but the examination should be conducted in a warm room and, if the atmosphere is chilly, a desk light shining directly on the stage of the microscope will be found advantageous. The light entering the field should be reduced so the refractile amebas stand out sharply.

The amount of the sample of feces to be examined needs some discussion. One deals here with a problem in probabilities and random sampling, although if suspicious portions in the specimen can be found from which to select material, a special problem of selective sampling also enters. The rough average weight of formed stools is about 65 Gm.; if one makes a proper

1. Dobell, Clifford: A Report on the Occurrence of Intestinal Protozoa in the Inhabitants of Britain with Special Reference to Entamoeba Histolytica, Med. Research Council, special report series **59**: 1-71, 1921.
2. Carter, H. F.; Mackinnon, Doris L.; Matthews, J. R., and Smith, A. M.: Protozoological Investigation of Cases of Dysentery Conducted at the Liverpool School of Tropical Medicine, Ann. Trop. Med. & Parasitol. **11**: 27-68 (June) 1917.
3. Svensson, R., and Linders, F. J.: The Chances of Detecting Infections with Intestinal Protozoa, Acta med. Scandinav. **81**: 267-324, 1934.

coverglass preparation, 22 by 22 mm., about 20 mg. of feces will be used. A rough average weight of stools following administration of salts is 170 Gm. Thus each coverglass affords about $\frac{1}{4,000}$ part of the specimen of a formed stool and about $\frac{1}{10,000}$ part of a stool following catharsis. This appears to be a small sample, but it is relatively 5,000 times more than the sample used to determine the erythrocyte count and about comparable to the sample from which urea in the blood is determined. If one examines two such preparations, although the material examined is doubled, the chance of finding a parasite is unfortunately not twice as great. Many items enter into this problem, but experience has shown clearly that one increases the chances of finding protozoa by taking samples from various parts of the stool and by making more than one coverglass preparation. If the material were homogeneous, of course, each preparation would have an equal chance of being positive, and one preparation would be as good as another. It is quite evident, therefore, that one should never examine less than two preparations, because the material is not homogeneous.

Probabilities of Finding a Protozoon in a Specimen of Stool

Concentration in Stool, Organisms per		Probability of Finding a Protozoon in the Field Examined* Fields Examined (22 by 22 mm.)				
Gm.	20 Mg.	¼ Field (2½ Min.)	½ Field (5 Min.)	1 Field (10 Min.)	2 Fields (20 Min.)	4 Fields (40 Min.)
5	0.1	0.025	0.049	0.095	0.181	0.330
10	0.2	0.049	0.095	0.181	0.330	0.551
15	0.3	0.072	0.139	0.259	0.451	0.699
20	0.4	0.095	0.181	0.330	0.551	0.798
25	0.5	0.118	0.221	0.394	0.632	0.865
50	1.0	0.221	0.394	0.632	0.865	0.982
100	2.0	0.394	0.632	0.865	0.982	0.9997
150	3.0	0.528	0.777	0.950	0.998	
200	4.0	0.632	0.865	0.982	0.9997	
250	5.0	0.714	0.918	0.993	0.99995	
300	6.0	0.777	0.950	0.998		
350	7.0	0.826	0.970	0.9991		
400	8.0	0.865	0.982	0.9997		
450	9.0	0.895	0.989	0.99987		
500	10.0	0.918	0.993	0.99995		

* The calculations are based on the assumption that a single complete field contains 20 mg. of the specimen and that this is a random sample of the stool in which the organisms are mixed at random. If four fields are examined and no organism is found, there is "practical certainty" that there are fewer than fifty organisms per gram in the stool, or fewer than 2.5 organisms in 20 mg. of preparation. Similarly, if two fields are examined and no organisms found, it is "certain" that there are less than 100 organisms per gram, and so forth.

After the material is selected and on the slide, the question of how long to examine the slide, with what magnification, and with what chances of finding parasites on the slide if they are actually present are all important problems.

For the initial examination of the smear, the lowest power under which protozoa can be recognized should be used, and all searching should be done with a mechanical stage. The particular organism is then identified by further study with higher powered lenses. One is not ready to begin the actual diagnosis of species until he can "spot" protozoa under the 16 mm. objective and a $\times 10$ eyepiece ($\times 100$ magnification). Herein lies the real difference in the results among many observers. Those who work entirely with lenses of higher power miss many parasites. The field of a 4 mm. lens is one-twelfth the size of a 16 mm. lens and that of the oil immersion lens is one one-hundredth the size of the low power lens. In addition, the plane or depth of focus is [redacted] igher power.

In arriving at the time [redacted] y to examine a preparation, measuring 22 by 22 mm., before deciding that it is negative one must first consider the number of fields on the slide. Allowing a 10 per cent overlap, there are about 160 fields at a magnification of 100 times. One who is experienced and is used to examining protozoa can detect the protozoa in a field if an average of nearly four seconds to the field is allowed. This means that to examine every field would require about ten minutes. If there were but one organism on the slide, it would surely be detected, since every field would be examined. Of course there is a personal factor involved as well as such factors as the evenness of the preparation and the quality of light but, since these vary so much and cannot be taken into a general calculation, computations are made on the assumption that if a protozoon should be in a field it would be seen. The accompanying table indicates the probabilities of finding a protozoon when different numbers or organisms are present in a 20 mg. sample of feces, over the ranges usully encountered. Since the area of the preparation examined and the time vary directly, one may conclude that the examination of one-fourth, one-half, or all the slide is equivalent to two and a half, five and ten minute examinations.

If there are very few organisms in the stool, such as, for example, an average of 0.1 of an organism per 20 mg. of feces, examining twice the number of preparations almost doubles the chance of finding an organism, provided the material is homogeneous. When the average number reaches a level as high as six organisms per 20 mg. of feces, however, the chances of finding an organism in a ten minute search are 0.998, or a failure of only two in 1,000 such examinations. Examining the slide only half so long or examining only half the slide still yields a chance of finding an organism in ninety-five of 100 such examinations. It is interesting to note that it would be better to spend the time on one slide rather than to divide equally the time between two slides, so far as the probability of finding an organism is concerned under the foregoing conditions, if the specimen is perfectly homogeneous as to distribution of organisms. There is another matter, however, which enters this picture and that is the fact that another sample may be better selected.

A question constantly arising is, after one has examined thoroughly a single slide or more than one slide and found no amebas, how many more slides should be examined before one may hope to encounter an organism, provided it is in the stool. These relations may be solved from the table. For example, if one examines four slides and finds no organism, one may be "sure" that there exists less than one ameba per 20 mg. of feces; if there had been as many as one per 20 mg., a single slide would have revealed the organism in 63 per cent of instances. Hence, if four preparations are negative, the concentration of protozoa in the stool is so low as to be almost impossible to detect. Similarly, if ten slides were negative, there would be less than 0.4 organism per 20 mg. of feces. Here again this presupposes a more or less equal distribution of organisms in the stool, and if special parts of the stool are selected the results will be varied. A number of interesting relations can be brought out from a study of the table, but in general one may say that if two coverglass preparations 22 by 22 mm. are examined for five minutes

each, being sure that each field is a new field, in the vast majority of cases if no organisms are found the specimen may be considered negative, provided of course the material has been properly selected and the examiner is competent. When the material is quite evidently not homogeneous and portions contain mucus and blood, a large series of slides should be made from different parts of the specimen, and spending less time on each preparation will give a higher chance of positive examinations than thoroughly examining fewer preparations, because of the introduction of the factor of selective sampling, which outweighs in such instances the mathematical possibilities indicated in the table. Doubling the time on each preparation would not pay, but examining new preparations would yield a higher degree of accuracy. It would be better, if possible, to obtain another specimen from the patient and then repeat the process of examination.

If one examined slides with the 4 mm. objective and the × 10 eyepiece, the time necessary to effect the same degree of accuracy, leaving out of consideration the difficulty of focal depth, would be about two hours for each examination. Under such conditions the slides would have to be ringed with petrolatum to prevent evaporation.

The time necessary to identify any given protozoon would vary with the ability and experience of the examiner and the nature of the organism. Flagellates and ciliates can be identified at a glance, and typical amebas do not require a very long time, but borderline forms and atypical forms may require lengthy observation and a time-consuming technic before positive identification can be made. Degenerating trophozoites give the greatest trouble and should not be too certainly identified.

IDENTIFYING SPECIES

The reader must be referred to standard textbooks and monographs dealing with the characteristics of unstained protozoa for the numerous details of their minute structure. Here it will be sufficient to call attention to a few major considerations. No one can be considered competent to diagnose the presence of Endamoeba histolytica unless he can identify the other four species of amebas, the four common flagellates, and one ciliate. One must be expert in recognizing cysts, precysts and trophozoites.

Trophozoites. — In the motile stage, specimens of Endamoeba histolytica usually are from 20 to 30 microns in diameter, but small races exist and these may have an average diameter no greater than 12 microns. The size is not a differential feature, except in a general way; Endolimax nana, Iodamoeba buetschlii, and Dientamoeba fragilis as a rule are smaller.

Without doubt the most striking thing about Endamoeba histolytica is its motion. It reminds one of the flowing of thick molasses. The important thing is its directional character, which pulls the ameba out in a bandlike form. The whole protoplasm flows along, the ectoplasm being almost unseen in rapidly moving forms. As time elapses, the motion becomes less characteristic, and explosive movements occur, with glasslike ectoplasmic blobs. The motion of all other amebas is nondirectional and not nearly so rapid, although comparison cannot be made unless one examines perfectly fresh, warm stools.

The content of the cytoplasm is a second characteristic. In Endamoeba histolytica the protoplasm is finely granular and almost homogeneous. If the amebas are from a patient with an acute case, or, sometimes, from a well purged carrier, erythrocytes may be seen within the cytoplasm. These probably never are ingested by other amebas, and for practical purposes one may, with assurance, call any ameba containing erythrocytes Endamoeba histolytica. Other species of amebas exhibit food vacuoles and ingest all manner of bacteria, fecal débris, and even other protozoa.

The third important characteristic is the nucleus. Because of its delicate nature and the opaqueness of the cytoplasm, the nucleus of Endamoeba histolytica is difficult to see; but by careful focusing and adjustment of the light, one frequently can make out the delicately beaded peripheral zone of chromatin, although rarely the central, delicate karyosome. The nucleus of Endamoeba coli is coarse, and a ring of chromatin is easily seen outlining it. Frequently, an eccentric karyosome can be distinguished.

Other Amebas.—The other three amebas are distinctly smaller than either Endamoeba histolytica or Endamoeba coli and, as a rule, quickly lose motility. They contain food vacuoles, with bacteria, and their nuclei are rarely seen in the fresh state.

One of the most confusing things in the examination of feces is the large number of objects which may be mistaken for amebas, and only great study, careful instruction and experience can protect the observer from error. The most confusing object is probably Blastocystis, a harmless, yeastlike organism present in many stools. Its peripheral "nuclei," however, clearly identify it. Large macrophages and even pus cells are also frequently mistaken for amebas.

Precystic Forms.—Precystic forms are almost impossible to distinguish in the fresh state, are devoid of food vacuoles and have thin, delimiting membranes. The nuclear characteristics remain constant but can be seen only in very favorable specimens.

Cysts.—The cysts of amebas are rather readily detected in the fresh material by their clear, glasslike appearance and gray-green color. The cysts of Endamoeba histolytica and of Endamoeba coli are almost always spherical, whereas those of Endolimax nana are usually ovoid. The cysts of Iodamoeba buetschlii are frequently irregular, whereas cysts of Dientamoeba fragilis are described by Kofoid as being spherical. The size varies with the species; cysts of Endamoeba coli are the largest, as a rule averaging from 12 to 18 microns, and those of Endamoeba histolytica average from 10 to 15 microns, with small races averaging as little as 5 microns and large races up to 20 microns. With favorable light, cigar-shaped chromidial bars may be seen in the cysts of Endamoeba histolytica and, occasionally, one may count the number of daughter nuclei in the cyst. In the fully developed cyst of Endamoeba histolytica, there are four such nuclei, whereas in that of Endamoeba coli there are eight. The structure of these nuclei is like that of the motile forms. Frequently the nuclei of cysts of Endamoeba histolytica are near four poles, suggesting two pairs, whereas in cysts of Endamoeba coli the nuclei are bunched in the center of the cyst.

IODINE STAINING

As an aid in diagnosing fresh amebas, compound solution of iodine (Lugol's solution) is very helpful. This may be used either to emulsify the fecal material or to run in under the coverglass while watching a

certain ameba under the lens. If one becomes skilful in the latter technic, much time can be saved, since the organisms stain brown with the iodine and are hard to distinguish from the background. Although iodine staining may be used to bring out the nucleus of the motile form, it has its greatest usefulness in identifying cysts. The nuclei can be readily counted and, under the oil immersion lens, the character of the nuclei can be seen in some cases. In addition, the mass of glycogen can be observed. In the early stages of cysts of both Endamoeba histolytica and Endamoeba coli, diffuse masses of glycogen exist, with a more abundant amount of glycogen in cysts of Endamoeba coli. In older cysts, it is rare to see the glycogen. Glycogen in several diffuse masses is usually seen in cysts of Endolimax nana whereas in cysts of Iodamoeba buetschlii the discrete spherical mass of glycogen is entirely diagnostic.

One must remember that while, as Lynch [4] remarks, the key to the diagnosis of cysts lies in the fact that those of Endamoeba histolytica have four nuclei and those of Endamoeba coli eight, at one stage every cyst of Endamoeba coli has four nuclei and every mature cyst of Endolimax nana four as well; in addition, sometimes, cysts of Endamoeba histolytica have more than four nuclei. It is the structure of the nucleus in the cyst that is finally determinative and not the number of nuclei alone. The fine, peripheral, beaded chromatin, and central, minute karyosome of the cyst of Endamoeba histolytica, as contrasted with the coarse band of chromatin, or large, heavy blobs, and heavy, eccentric karyosome, with granules between it and the periphery of the nucleus, in that of Endamoeba coli, are the true criteria for identification.

PERMANENT STAINED PREPARATIONS

In all cases of doubt, or when evidence is to be kept, permanent, stained slides should be made. One may, in any large routine series, expect to correct about 10 per cent of diagnoses of Endamoeba histolytica by properly prepared, stained slides. However, by carefully choosing the specimens for such checking, one can obtain satisfactory results by staining only a relatively few slides. As a rule, it is harder to find amebas on these slides than in fresh smears, and the labor of preparation and searching greatly discourages their general use.

Many methods have been proposed and many modifications offered, but the one most generally used and most satisfactory is iron hematoxylin staining following fixation in Schaudinn's fluid. The following brief outline gives a satisfactory technic:

1. Make a thin smear on a very clean slide and, when the edges begin to dry and while the preparation is still moist, plunge the slide into Schaudinn's fixative.
2. Fix thirty minutes.
3. Wash in running water for thirty minutes to one hour.
4. Treat slide with dilute solution of iodine.
5. Rinse.
6. Pass successively through alcohol solutions, 50 per cent, 70 per cent and 95 per cent, respectively, and harden in 95 per cent alcohol for one hour.
7. Return to water for five minutes.
8. Mordant in 2 per cent iron alum, twenty minutes.
9. Wash with six changes of water.
10. Stain in 0.5 per cent hematoxylin, fifteen minutes.
11. Wash and decolorize in 2 per cent iron alum until nuclear detail is clear (under the microscope).
12. Wash thoroughly and to the last rinse water add a drop of ammonium hydroxide.
13. Dehydrate, using acetone in which a small amount of eosin has been added instead of absolute alcohol.
14. Place in xylene and mount in balsam. If the proper amount of eosin is used, it will greatly facilitate the identification of amebas which, not taking the eosin as readily as the background, stand out sharply against it.

By this method of staining the diagnostic details of all species of amebas are clearly revealed, and a final decision as to diagnosis may be reached when the organisms are in either the motile or the cystic stage. However, it is important to stress the point that for motile forms the slides must be fixed before the amebas have time to degenerate. Further, the diagnosis must rest, as in examining fresh material, on observing many individuals and sizing up the whole situation, it being remembered that frequently patients may harbor two or more species of amebas.

CONCENTRATION METHOD

In examining formed stools for cysts, one may advantageously resort to a concentration method. A satisfactory method is to emulsify about 2 Gm. of feces in 15 cc. of physiologic solution of sodium chloride in a conical centrifuge tube. The material should be spun for one minute at a moderate rate and the sediment in the bottom of the tube examined. If coarse particles are present in the emulsion, they should be strained out through gauze before centrifugation. One may examine the sediment either unstained, stained with iodine, or fixed; iron hematoxylin stained slides may be prepared as previously outlined.

EXAMINATION OF MATERIAL OTHER THAN FECES

Under certain conditions it will be found advantageous to examine material obtained directly from ulcers in the rectum and colon by means of the proctoscope. One should have a wire curet available and scrape out the crater of an ulcer, placing the material on a slide and applying a coverglass. If the ulcer is amebic, one will observe many organisms of Endamoeba histolytica in the mucus and in the bloody exudate; these are in every respect typical and usually contain numerous erythrocytes. Excellent permanent preparations may be made from such material.

Tissue for diagnosis of amebiasis may be conveniently obtained through the proctoscope, but this is rarely indicated. One may be called on to diagnose a surgical specimen or material at necropsy. Here again the demonstration of typical amebas is essential for the positive diagnosis. The type of ulcer is more or less characteristic, with its overhanging edges and undermined deep excavation. However, these characters are not sufficient basis on which to make a diagnosis, and very early lesions do not show such characteristics.

The proper fixative is Schaudinn's fluid and, after allowing from two to six hours for fixation, the material should be handled in the usual way for paraffin sections. Serial sections are not often necessary, but in any event many sections should be made. At least some should be stained with iron hematoxylin. The usual hematoxylin-eosin stain following fixation in formaldehyde is worthless and leads to serious errors.

4. Lynch, K. M.: Protozoan Parasitism of the Alimentary Tract, New York, Macmillan Company, 1930.

Recently, Meriwether [5] has used Best's stain on formaldehyde-fixed tissue with striking success, although the details of the nuclei are not so good as with iron hematoxylin staining.

If tissue is to be examined from a hepatic abscess, a part of the wall should be fixed and sectioned; the amebas will lie in the so-called intermediary zone between the pus and the injured hepatic parenchyma.

Since amebas have been found from other parts of the body besides the bowel, one may have material other than feces to examine. The amebas found in discharges from sinuses and in sputum are vegetative forms and should be sought by examining material fresh from the source. In examining pus from a suspected amebic, hepatic abscess, it should be remembered that the organisms are frequently not in the pus first aspirated from the abscess but are embedded in the more fixed and unresolved margins of the lesion, and they can be obtained only by lightly scraping the walls of the abscess. After drainage has been established, the organisms appear in the pus and can readily be demonstrated in wet smear preparations. One should remember that large pus cells and other reaction cells can resemble amebas and that rigid criteria must be applied to each object under suspicion before a positive diagnosis is made.

CULTURAL METHODS

St. John [6] was probably the first to report making a diagnosis of amebiasis by a cultural method when direct examination of the stool gave negative results. Since then, many have reported the value of such a method. Some workers have reported finding more positive specimens by this method than by smears; for example, Craig and St. John,[7] Bundesen and others,[8] and Tsuchiya,[9] who found almost twice as many cases of Edamoeba histolytica by the cultural method as by that of direct smear. Others, such as Magath and Ward,[10] and Miller,[11] have reported the reverse. Still another group of investigators have reported other relations. Thus Johns and Tripoli [12] reported almost precisely checking cultures and smears in a series of cases; seven months later, however, Johns [13] reported that of fifty cases of Endamoeba histolytica, in forty-nine the direct smear was positive and in only thirty-nine was the culture positive. In only one case was diagnosis made by culture and not by direct smear. Svensson and Linders diagnosed infestations of Endamoeba histolytica in 94 per cent of their cases by culturing a single stool following the administration of salts. They further reported growths in 84 per cent of the cases of infestation with Endamoeba coli, in 51 per cent of those of Endolimax nana, in 60 per cent of those of Iodamoeba buetschlii, and in all of those of Dientamoeba fragilis.

Poindexter [14] concluded "the cultural method as described to be superior in the interests of accurate diagnosis, because in doubtful cases Endamoeba histolytica may be more easily differentiated from Endamoeba coli in the vegetative stage than in the encysted stage." However, he did not comment on the fact that in his study he identified Endamoeba histolytica sixty-six times in 564 specimens by direct smear, and only fifty-three of these grew by his cultural methods, a loss in the cultures of more than 20 per cent.

A variety of mediums have been used, including such simple mixtures as salt solution and serum. A medium favored by many is a slant of liver infusion agar to which is added, as an overlayering fluid, a mixture of one part serum to seven parts of salt or Locke's solution. To this is then added a small loopful of sterile, rice starch. An egg base may be substituted for the liver-agar and egg-white mixtures in salt solution for the serum mixture. Why some workers fail to obtain uniform growth is not clear, but it is suggested that the quality of the starch may be the crux of the situation and that this question should be further investigated. The cultures reported by Bundesen and others were made from formed stools, but most other investigators have stressed the necessity for a very fresh, warm stool. Growth appears in from twenty-four to forty-eight hours. Overgrowth of harmful bacteria and Blastocystis frequently spoils the cultures.

The identification of the amebas in culture is by no means easy, nor have rigid criteria for their identification been as yet set up by any one. How Svensson and Linders identified so many different species is not indicated by them, and if they were correct it suggests that others have confused Endamoeba histolytica and Dientamoeba fragilis at least, if not other forms. St. John apparently depended on the motility and shape of the moving ameba, but Martin [15] pointed out the marked similarity between cultured organisms of Endamoeba histolytica and the trophozoites of Endamoeba coli. Some apparently consider any ameba growing in culture as Endamoeba histolytica, believing that other forms rarely if ever grow. If Svensson and Linders are correct in their results, such is not the case and, if this is the sole criterion, numerous errors are likely to occur in such diagnoses. One should also remember that free-living amebas may appear in the cultures and that the utmost caution and greatest experience is necessary before one may safely identify amebas in culture; nevertheless, it is a method well worthy of utilizing.

It is evident to any one who has given consideration to the comparison of smear and culture methods that the skill and persistence of the microscopist will greatly determine how many more cultures than smears are found positive. In at least one laboratory it was evident that experience with the low power lenses resulted in finding more by direct smear than by culture when, previously, using the higher power lenses had resulted in the discovery of nearly twice as many infestations by culture as by smear.

5. Meriwether, L. S.: Identification of the Amebas in Tissue, Proc. Staff Meet., Mayo Clin. **9**: 95-96 (Feb. 14) 1934.
6. St. John, J. H.: Practical Value of Examination for Endamoeba Histolytica by Culture, J. A. M. A. **86**: 1272 (April 24) 1926.
7. Craig, C. F., and St. John, J. H.: The Value of Cultural Methods in Surveys for Parasitic Amebae of Man, Am. J. Trop. Med. **7**: 39-48 (Jan.) 1927.
8. Bundesen, H. N.; Rawlings, I. D., and Fishbein, W. I.: The Health Hazard of Amebic Dysentery: Report of an Outbreak, J. A. M. A. **101**: 1636-1638 (Nov. 18) 1933.
9. Tsuchiya, H.: Further Studies on the Cultivation of Endamoeba Histolytica and a Complement Fixation Test for Amebiasis, J. Lab. & Clin. Med. **19**: 495-504 (Feb.) 1934.
10. Magath, T. B., and Ward, Charlotte B.: Laboratory Methods of Diagnosing Amebiasis, Am. J. Hyg. **8**: 840-857 (Oct.) 1928.
11. Miller, M. W.: Difficulty in Cultivation of Endamoeba Histolytica, Proc. Soc. Exper. Biol. & Med. **25**: 762-763 (May) 1928.
12. Johns, F. M., and Tripoli, C. J.: The Incidence of Infection with Endamoeba Histolytica in Louisiana as Determined by Comparative Microscopic and Cultural Methods, New Orleans M. & S. J. **82**: 224-227 (Oct.) 1929.
13. Johns, F. M.: Cultural Methods and Direct Microscopic Examination in the Diagnosis of Pathogenic Amebas, South. M. J. **23**: 236-238 (March) 1930.
14. Poindexter, H. A.: The Puerto Rican Strain of Endamoeba Histolytica, Puerto Rico J. Pub. Health & Trop. Med. **9**: 31-36 (Sept.) 1933.
15. Martin, D. L.: The Lesions in Experimental Amebic Dysentery, Arch. Path. **10**: 349-385 (Sept.), 531-579 (Oct.) 1930.

COMPLEMENT FIXATION

The most recent method of diagnosing amebiasis is by complement fixation, described by Craig.[16] The method at the present time has been limited to a few investigators and cannot be considered ready for routine application. The antigen is made by growing large numbers of amebas in cultures and making an alcoholic extract of them. After proper titration, the test is conducted along the lines of routine complement fixation tests. Craig used his antigen undiluted, and his best antigens in antigenic amounts approached closely their anticomplementary unit. This, of course, gives a small working distance, so to speak, and requires great care in setting up the test and caution in its interpretation. Tsuchiya asserted that he had made a better antigen and employed a fourth of the anticomplementary unit of a 1:100 dilution. He concluded that a negative test was significant and valuable in ruling out amebiasis, but while he stated that "a positive serologic test also seems to be quite specific in demonstrating the presence of Endamoeba histolytica," his protocols do not warrant such a conclusion. Of seventeen positive tests, four were in cases in which other laboratory tests for amebiasis were negative and, clinically, the diagnosis of ulcerative colitis had been made. There was one patient with amebas in the stools and a negative complement fixation test; hence, the check was actually only thirteen of eighteen patients. The error on the positive side alone was 23 per cent.

The test has great theoretical interest and warrants much more study but is not yet ready to become a routine addition to the clinical laboratory and must, for a while at least, remain in the hands of the most experienced.

SUMMARY AND CONCLUSIONS

It is evident that the laboratory diagnosis of amebiasis requires special knowledge and skill and should not be attempted except by those adequately trained and with a large measure of experience. The problems involved are quite comparable to those involving diagnosis of tissue. The diagnosis of amebiasis should be made only by those specially qualified.

The direct smear method is adequate in the hands of those properly trained in almost all cases but, if doubt exists, one should resort to fixed and stained preparations. Whether one uses formed stools or those resulting from catharsis will depend on the individual problem. Whichever is used, the limitations of the particular method must be clearly recognized.

Culture methods should be used in laboratories qualified to identify amebas, but, for the usual routine, cultures are not necessary, provided the examiner thoroughly knows how to make proper direct examinations. The cultural characteristics of various amebas growing in these cultures have yet to be clearly described, and a series of animal experiments to determine the types in a large series is greatly needed.

Until the complement fixation method is simplified, it is not suitable for routine tests.

Seventy-five per cent of infestations with Endamoeba histolytica can be found by examining a single stool following catharsis with magnesium sulphate, whereas only a third of the infestations will be found by examining a single formed stool. It will require from eight to ten formed stools to establish the same number of infestations as three stools following catharsis.

16. Craig, C. F.: The Technic and Results of a Complement Fixation Test for the Diagnosis of Infections with Endamoeba Histolytica, Am. J. Trop. Med. **9**: 277-296 (Sept.) 1929.

THE TREATMENT OF AMEBIASIS

CLINICAL LECTURE AT CLEVELAND SESSION

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It is my purpose to discuss the treatment of amebiasis in strictly practical terms as condensed from soundly supported scientific evidence and personal experience. No attempt will be made, therefore, to review the history or describe all the methods that have been advised. Since the introduction of ipecac into Europe in 1672, therapy has been influenced by three tendencies. In the first place, ideas of etiology and methods of diagnosis have improved. In the second place, there was a tendency to use complex formulas and substances found useful in other diseases the causes of which were biologically related, as in the case of quinine. Finally there has been the tendency to seek active principles, simple preparations and the exact methods of chemotherapeutic study, with attention to the relation between chemical structure and physiologic action.

MAJOR ANTIAMEBIC DRUGS

Leake [1] states that "few of the agents exploited for use in this condition have sufficient experimental background to justify even controlled clinical trial in human beings." He [2] lays down the dictum that "physicians are not justified in using new medicinals in their daily practice until . . . favorable reports have been published from trustworthy chemical, pharmacologic and clinical sources." With these criteria in view, I shall briefly summarize the chief drugs that have received widespread use in amebiasis. Leake [1] has made a pharmacologic classification of the major drugs that have been used in the treatment of amebiasis. He divides them into four groups: (I) alkaloids such as in ipecac and kurchi (cinchona might have been added), (II) organic arsenicals, such as acetarsone ("stovarsol") and carbarsone, (III) oxyquinoline derivatives such as chiniofon ("yatren") and vioform and (IV) miscellaneous antiseptics and astringents such as the alkyl resorcinols and bismuth compounds.

GROUP I

In group I, I will consider ipecac and its chief alkaloid, emetine. Quinine has been highly recommended but has not withstood the test of time. Kurchi preparations are less effective in my experience, although Acton and Chopra [3] in Calcutta consider them useful. Ipecac powder plays an important part in the history of amebic therapy. Its use today is archaic and completely ignores the tendencies in therapeusis already noted. Its efficacy depended entirely on its content of emetine, which has great advantages in accuracy, ease of administration and effectiveness. The use of ipecac powder at present is therefore to be condemned entirely.

Emetine was first isolated and suggested for use in amebic dysentery by Vedder [4] in the Philippines in

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1. Leake, C. D.: Chemotherapy of Amebiasis, J. A. M. A. **98**: 195 (Jan. 16) 1932.
2. Leake, C. D.: Pharmacologic Evaluation of New Drugs, J. A. M. A. **93**: 1632 (Nov. 23) 1929.
3. Acton, H. W., and Chopra, R. N.: Kurchi Bismuthous Iodide—Its Value in Treatment of Chronic Amebic Infections of the Bowels, Indian M. Gaz. **64**: 481 (Sept.) 1929.
4. Vedder, E. B.: An Experimental Study of the Action of Ipecacuanha on Amoebae, Far Eastern A. Trop. Med., Tr. 2d Biennial Congress, Hongkong, 1912, p. 87.

1912. The following year, Rogers [5] in Calcutta reported its clinical use in acute cases with remarkable and very quick relief of symptoms but, as later shown, amebas persisted after symptoms subsided. These results were soon confirmed by a host of observers. I will now summarize the toxic dangers of emetine and evaluate its position in present-day treatment.

It was early noted clinically that excessive use of emetine was followed by accentuation or recurrence of diarrhea, sometimes attended by nausea, by peripheral palsy and edema, and by weakness and irregularity of the heart, and that locally it was irritant to the tissues. Few adequate reports on human toxicity have been made. Leake [1] summarizes the published data to 1932 on the quantitative toxicity of emetine hydrochloride, with the average figures agreeing closely with the results of Anderson and Leake [6] in cats and rabbits. Similar observations were made in the case of emetine bismuth iodide, emetine antimony iodide, "auremetine," and iso-amylcephaeline phosphate. It seems safe to conclude that the effective dosage of all preparations containing emetine overlaps seriously the toxic range of the alkaloid. Dobell and Bishop [7] proved this in monkey amebiasis, in which a dosage sufficient to be effective was attended by toxic symptoms in 80 per cent of the animals treated. Levy and Rowntree [8] reported a fatality in man at a dosage of about 25 mg. per kilogram. This range was the same as that reported by Leake [1] as lethal in experimental laboratory animals and by Leibly [9] in a human case of fatal emetine poisoning. Leake [1] found a striking uniformity of lethal dosage in animals, regardless of the method of administration, except by vein, when it is many times as toxic, and regardless of whether given in a single dose or in divided doses over a relatively long time. He says: "These data indicate that emetine is detoxified or eliminated very slowly indeed, and, in conjunction with experimental and clinical observations, they point to its 'fixation' in some tissue of relatively the same functional significance in all genera, with perhaps quantitative morphologic damage, which, if extensive enough after a certain dosage, leads to such impairment of function that death may follow."

Chopra, Ghosh and De [10] in 1924 concluded that emetine was a general protoplasmic poison with selective action on certain organs in the rabbit. They found that one of the earliest tissues to be affected is the parenchyma of the heart muscle, the changes being (*a*) cloudy swelling of muscle fibers with disappearance of transverse striations, (*b*) shrinkage of muscle fibers and (*c*) atrophy of muscle fibers and their replacement by connective tissue. They state that the occurrence of petechial hemorrhages at the site of emetine injection indicates local damage to the endothelium of the capillaries. The liver and kidneys are affected later, showing chiefly congestion and fatty infiltration of the parenchyma. Young and Tudhope [11] report similar observations and in addition substantiate their claim that emetine experimentally does not affect nerves or nerve sheaths but does cause a myositis by action on muscle fiber protoplasm directly leading to muscular palsy.

Rinehart and Anderson [12] at the University of California have confirmed and extended these observations, showing that lethal or sublethal doses of emetine caused severe injury to the heart muscle in rabbits. Morphologic changes appeared after an interval of time. In animals that survived three days or longer, necrosis was seen in some fibers and degenerative swelling in the remainder. "This resulted in a rarefaction of the heart muscle and in focal proliferations of the interstitial tissue in response to the necrotic muscle fibers. A more chronic intoxication produced with divided lethal doses of emetine hydrochloride resulted in small cellular scars in the myocardium centered about necrotic muscle fibers."

It may be concluded, therefore, that emetine is unsatisfactory and dangerous for routine use for three reasons: first, because effective dosage lies within its toxic range; [6] second, because of proved damage to the heart muscle in dosages little above therapeutic amounts, with the danger that smaller dosage may mean only a smaller damage instead of freedom from damage, and the added danger of permanent impairment due to the scarring process evoked in cardiac muscle; and, third, because of the low effectiveness of this drug in clinically safe amounts against amebas, even though it is an excellent adjuvant for relief of acute symptoms. The need for cautious administration being recognized, emetine has still an important therapeutic place in liver damage, in malignant or severe acute dysentery and in surgical amebic lesions, in which its use has two decided advantages: (*a*) It is much less toxic for the liver than other recommended drugs, and (*b*) it gives quick symptomatic control, preparing the way for more curative drugs. This opinion is supported by Craig,[13] who says that emetine is of comparatively little value in actually curing amebiasis although most efficient in curing symptoms. Cort,[14] on the basis of wide experience in Siam, believes that emetine is more specific for hepatic than for intestinal amebiasis. Johns [15] considers that emetine and its compounds have at times certain disadvantages "either from the standpoint of difficulty in administration, toxicity, or ineffectiveness in establishing a permanent cure." Manson-Bahr [16] believes that emetine, uncombined with other treatment, is insufficient to eradicate amebic infection, although of great value in acute stages.

GROUP II

Leake's classification of group II includes organic arsenicals. The arsphenamine type of arsenical is not considered here because of the difficulty of administration, toxicity, expense, unproved effectiveness and availability of more satisfactory arsenicals. Out of a considerable number of other arsenicals that have been

5. Rogers, Leonard: The Rapid Cure of Amoebic Dysentery and Hepatitis by Hypodermic Injections of Soluble Salts of Emetine, Brit. M. J. **1:** 1424 (June 22) 1912; Further Experience of the Specific Curative Action in Amoebic Disease of Hypodermic Injection of Soluble Salts of Emetine, ibid. **2:** 405 (Aug. 24) 1912; Amoebic Colitis in India; Prevalence, Diagnosis and Emetine Cure, Lancet **2:** 1062 (Oct. 19) 1912; Sixty Cases of Amoebic Dysentery Illustrating the Treatment by Ipecacuanha and Emetine, Respectively, Indian M. Gaz. **47:** 421, (Nov.) 1912.

6. Anderson, H. H., and Leake, C. D.: The Oral Toxicity of Emetine Hydrochloride and Certain Related Compounds in Rabbits and Cats, Am. J. Trop. Med. **10:** 249 (July) 1930.

7. Dobell, C., and Bishop, A.: Action of Emetine on Natural Amoebic Infections in Macaques, Parasitology **21:** 446, 1929.

8. Levy, R. L., and Rowntree, L. G.: On the Toxicity of Various Commercial Preparations of Emetine Hydrochloride, J. Pharmacol. & Exper. Therap. **8:** 120, 1916.

9. Leibly, F. J.: Fatal Emetine Poisoning Due to Cumulative Action, Am. J. M. Sc. **179:** 834 (June) 1930.

10. Chopra, R. N.: Ghosh, B. N., and De, P.: Toxicity of Emetine, Indian M. Gaz. **59:** 338 (July) 1924.

11. Young, W. A., and Tudhope, G. R.: The Pathology of Prolonged Emetine Administration, Tr. Roy. Soc. Trop. Med. & Hyg. **20:** 93-99 (March-May) 1926.

12. Rinehart, J. F., and Anderson, H. H.: Effect of Emetine on Cardiac Muscle, Arch. Path. **11:** 546 (April) 1931.

13. Craig, C. F.: Symptomatology, Diagnosis and Treatment of Carriers of E. Histolytica, J. A. M. A. **90:** 1345 (April 28) 1928.

14. Cort, E. C.: Amebiasis of the Liver, J. A. M. A. **90:** 2005 (June 23) 1928.

15. Johns, F. M.: Amebiasis with Special Reference to Its Treatment with Iodoxy-Quinolin Sulphonic Acid, M. Clin. North America **13:** 1307 (March) 1929.

16. Manson-Bahr, P. H.: Recent Developments in Treatment of Amebiasis, Trop. Dis. Bull. **22:** 259, 1925.

recommended or suggested on theoretical grounds, I shall note only two, acetarsone and carbarsone.

Acetarsone ("stovarsol") was probably the first organic arsenical administered by mouth as an amebacide. This report was by Marchoux [17] in 1923, after this drug had been recommended for oral use in syphilis by Fourneau in 1921. Acetarsone was introduced into this country in 1924 and has been widely used. However, it is too toxic [18] in doses that have reasonable clinical effectiveness, and arsenic poisoning has followed its use in many cases.[19]

Carbarsone is a name of convenience for 4-carbaminophenyl arsonic acid, introduced in 1932 by Reed, Anderson, David and Leake [20] at the University of California. It is odorless, tasteless, and highly insoluble in water but soluble in alkaline aqueous solutions. Given by mouth, it is absorbed and excreted at about the same rate as acetarsone.[21] "Experimentally it is less toxic than acetarsone but more amebacidal, its 'therapeutic index' being about eight times as favorable as acetarsone." [22] In clinical use in my service carbarsone has shown no evidence of injury to the optic tract in about 400 patients who have received it to date. "As with arsenicals generally, it is contraindicated in the presence of kidney or liver disease and hence should not be used in amebic hepatitis." [20] In therapeutic dosage no toxic symptoms or signs were noted in extensive and well controlled animal experiments. A total dosage of 75 mg. per kilogram of body weight can be divided into two or three doses each day for a period of at least ten days. Carbarsone has been shown to have a high therapeutic efficiency, low toxicity, availability for oral administration and low cost. These desiderata make it, in my opinion, one of the most valuable of the antiamebic drugs.

GROUP III

The oxyquinoline derivatives offer two drugs for special consideration, chiniofon ("yatren") and vioform.

Chiniofon was introduced as a treatment for amebiasis by Mühlens and Menk [23] in 1921. It has received excellent reports from O'Connor and Hulse,[24] for example. Anderson, David and Koch,[25] however, found chiniofon not so effective experimentally as the higher halogenated oxyquinoline, vioform. O'Connor and Hulse [24] found that liver abscess seemed not to be affected by chiniofon orally and believed that the drug had a direct action on amebas in the intestinal tract only. The cost is considerably higher than that for other equally or more effective drugs. Craig [13] believes that chiniofon therapy requires bed rest, administration both by mouth and by rectum, and a careful diet. Its low amebacidal activity makes a large dosage necessary, about 200 0.25 Gm. pills by mouth being an average course. Two fatal cases with evidence of liver damage have been reported following the use of "yatren" intravenously in actinomycosis.[26] Apparently even small doses are toxic, given in this manner.

Vioform (iodochloroxyquinoline) was used on theoretical grounds in amebiasis of macaque monkeys experimentally by Anderson and Koch.[27] In monkey amebiasis, they report vioform to be the most satisfactory of all the common amebacides, in completely and promptly eliminating E. histolytica. Toxicity studies in rabbits showed no tissue damage in therapeutic dosage. In lethal amounts liver damage was found, and the drug therefore should not be used in the presence of impaired liver function. Vioform has been used in human cases of amebiasis by David, Johnstone, Reed and Leake [28] with results in their hands superior to chiniofon. Anderson and Reed [29] reported sixty cases of amebiasis treated with vioform orally. Three of these showed evidence of gastrointestinal irritation. Vioform is insoluble, but the soluble hydrochloride is irritating to mucous membranes in a concentration of 1 : 500. Rectal use is not recommended on this account. In the presence of gastric hyperacidity it may be that enteric coated capsules will prevent irritation. Vioform seems more satisfactory than chiniofon in amebacidal activity, in the need of a smaller dosage at less cost and in requiring neither bed rest nor rectal administration. It seems less satisfactory than carbarsone, in that it appears more apt to cause gastrointestinal irritation, seems somewhat less effective in active dysentery, and lacks the definite tonic and stimulating action of carbarsone. As an adjunct or in alternation with carbarsone it seems to fill an important place in amebic therapy.

GROUP IV

In group IV I shall consider bismuth compounds, certain alkyl resorcinols, and some astringents.

Bismuth subnitrate in massive doses has been used and recommended by many authors, notably by James and Deeks.[30] Anderson and Reed point out that reports of nitrite poisoning are not uncommon after ingestion of sufficient quantities of bismuth subnitrate to control diarrhea. Fatal results have been reported both in infants and in adults. Roe,[31] in a very complete review of the subject, says: "Since most individuals can tolerate huge doses without cyanosis and since methemoglobinemia is most likely to occur in patients who have intestinal putrefaction, nitrite poisoning and methemoglobinemia appear to be dependent on the presence of certain putrefactive bacteria in the intestine, or on an idiosyncrasy to certain drugs (Sollmann, van den Bergh and Beck). Large doses of nitrates taken by mouth may produce collapse, but rectal injections of smaller doses may cause nitrite poisoning much more quickly than that from oral administration. Children

17. Marchoux, E.: Le stovarsol guérit rapidement la dysenterie amibienne, Bull. Soc. path. exot. **16:** 79, 325, 1923.
18. Anderson, H. H., and Leake, C. D.: Toxicity of Acetarsone, Proc. Soc. Exper. Biol. & Med. **27:** 267 (Dec.) 1930.
19. Bender, W. L.: Stovarsol Poisoning, Am. J. M. Sc. **174:** 819 (Dec.) 1927.
20. Reed, A. C.; Anderson, H. H.; David, N. A., and Leake, C. D.: Carbarsone in the Treatment of Amebiasis, J. A. M. A. **98:** 189 (Jan. 16) 1932.
21. Chen, M. Y.; Anderson, H. H., and Leake, C. D.: Rate of Urinary Excretion After Giving Acetarsone and Carbarsone by Mouth, Proc. Soc. Exper. Biol. & Med. **28:** 145 (Nov.) 1930.
22. Leake, C. D.; Koch, D. A., and Anderson, H. H.: Effect on Biologic Activity of Substituting Sulphur for Oxygen in an Organic Arsenical Compound, Proc. Soc. Exper. Biol. & Med. **27:** 714 (Oct.) 1930.
23. Mühlens, P., and Menk, W.: Ueber Behandlungsversuche der chronischen Amöbenruhr mit Yatren, München. med. Wchnschr. **68:** 802 (June 30) 1921. Mühlens, P.; 5 Jahre Behandlung der Amöbenruhr mit "Yatren 105," Arch. f. Schiffs-u. Tropen-Hyg. **29:** 491 (Oct.) 1925.
24. O'Connor, F. W., and Hulse, C. R.: Treatment of Amebiasis with Anayodin, XIX Ann. Rep. United Fruit Company, Med. Dept., 1930. Mackie, T. T.: Iodoxyquinolin Sulphonic Acid (Anayodin) in Treatment of Intestinal Amoebiasis, ibid.
25. Anderson, H. H.; David, N. A., and Koch, D. A.: Effects of the Halogenation of Oxyquinoline on Biological Activity, Proc. Soc. Exper. Biol. & Med. **28:** 484 (Feb.) 1931.
26. Maxon, Hans: Zwei Fälle von Leberschädigung nach Yatren Behandlung, Ztschr. f. Chir. **60:** 879 (April 15) 1933.
27. Anderson, H. H., and Koch, D. A.: Iodochloroxyquinoline (Vioform N. N. R.) as an Amebacide in Macaques, Proc. Soc. Exper. Biol. & Med. **28:** 838 (May) 1931.
28. David, N. A.; Johnstone, H. G.; Reed, A. C., and Leake, C. D.: The Treatment of Amebiasis with Iodochlorhydroxyquinoline (Vioform N. N. R.), J. A. M. A. **100:** 1658 (May 27) 1933.
29. Anderson, H. H., and Reed, A. C.: Untoward Effects of Antiamebic Drugs, Am. J. Trop. Med. **14:** 269 (May) 1934.
30. James, W. M., and Deeks, W. E.: Etiology, Symptomatology and Treatment of Intestinal Amebiasis, Proc. Internat. Conf. Health Problems in Tropical America, (United Fruit Company) 1924, p. 271; Am. J. Trop. Med. **5:** 97 (March) 1925. James, W. M.: Treatment of Amebiasis, J. A. M. A. **102:** 1175 (April 7) 1934.
31. Roe, H. E.: Methemoglobinemia Following the Administration of Bismuth Subnitrate: Report of Fatal Case, J. A. M. A. **101:** 352 (July 29) 1933.

appear to be more susceptible than adults to nitrite poisoning." This conclusion is important with reference to treatment of intestinal amebiasis, in which a bacterial colitis is so prone to coexist. Bismuth subcarbonate is equally effective on pharmacologic grounds and, in my experience, avoids the definite hazards of the subnitrate. I have had no untoward effects from bismuth subcarbonate and have found it to be of definite value as an adjunct in treatment.

Of the alkyl resorcinols, heptylresorcinol was suggested in antiamebic therapy by Faust.[32] I was unable to confirm his results. The toxicity of this group seems to increase with increase in size of the alkyl radical.[33] Of the three readily available drugs of this series, the lowest alkyl radical, hexylresorcinol, would seem most worthy of further study. So far, results of its use in amebiasis do not seem to justify recommending it. Other astringents, such as tannates, are of definite symptomatic usefulness.

In general, the criteria of satisfactory therapy in amebiasis may be summarized as follows:[20] Drugs used should be clinically nontoxic, should be highly curative without adjuvants, should be available for oral administration, should interfere little, if at all, with the usual activities of the patient, and should be of low cost. These principles must receive full weight in outlining a scheme of treatment. The physician is justified only and strictly in using those drugs which most nearly fulfil these requirements.

PRACTICAL TREATMENT

In outlining an actual program of treatment, James's[34] dictum must be kept in mind. "Whether it is always a tissue parasite, or whether it can live harmlessly for long intervals in the lumen of the bowel, histolytica is invariably an enemy of its host, actively or potentially, and should be treated as such whenever and wherever found." It is assumed that spontaneous cure does not take place and that the one portal of entry is through the colon. The clinical rule should be to treat effectively every diagnosed case of amebiasis. The disease is transferred by cysts alone. Cysts must be swallowed to cause infection. Food, drink, fingers and utensils therefore offer the only means of transfer. Isolation of the patient is unnecessary, but care in personal hygiene, avoidance of fecal contamination, and clean food and drink are essential.

The scheme of treatment must be based on the colonic infection. In general, seven types of clinical picture must be considered from the standpoint of treatment to be selected: (1) dysentery with acute, malignant onset and course; (2) dysentery or diarrhea with subacute onset and course; (3) chronic amebiasis with recurring, inconstant or absent symptoms; (4) extra-intestinal abscess or ulceration; (5) complications of other diseases or of a surgical nature, and (6) sequels such as sprue, chronic simple colitis, chronic ulcerative colitis, cancer, chronic infections such as tuberculosis, and mechanical defects such as stricture. To complete the classification, a final group must be added, (7) comprising toxic results of drugs used.

1. Dysentery with acute, malignant onset and course requires immediate diagnosis and unusually prompt treatment. Anderson and I have had excellent results with the rectal use of carbarsone,[35] which allows a relatively high concentration of the drug to be applied directly to the diseased area. A cleansing soda enema is followed in one hour by instillation into the rectum of 200 cc. of warm 2 per cent sodium bicarbonate solution containing 1 per cent carbarsone (supplied by Eli Lilly & Co. in 2 Gm. vials). Usually a quick sedative effect is procured by the previous administration of sodium amytal (0.2 Gm.) orally to insure sleep and facilitate retention of the enema over night. If the enema is expelled before morning, the treatment is repeated until at least five enemas have been retained over night. Prompt symptomatic relief is the rule.

If such a course is not possible, or as an alternative and less desirable treatment, emetine hydrochloride may be given hypodermically (never intravenously) in a single daily dose of 0.065 Gm. (1 grain) to a total of six doses. At the most, these six one grain doses may be followed by six doses of one-half grain (0.032 Gm.) each. The ultimate total must never exceed 10 mg. per kilogram of body weight, or 0.65 Gm. (10 grains) for a man of average weight. Other forms of emetine, and especially ipecac, are not advised.

After the initial course indicated, the treatment should proceed as described later for chronic amebiasis.

In this clinical group, often attended by fever and prostration, the patient should be in bed, on a diet of boiled milk, white bread, stale or toasted, soft cooked eggs, gelatins, tea and white rice. Feedings should be at intervals of two and one-half hours. Adequate rest should be secured by the use of sodium amytal or sodium pentobarbital by mouth or hypodermically. Symptomatically for severe colic, excessive frequency of bowel movements and bleeding, the physician may administer equal parts of either dicalcium phosphate or tribasic calcium phosphate and bismuth subcarbonate in 4 Gm. doses from three to ten times daily. Rarely atropine sulphate ($\frac{1}{150}$ grain, or 0.0003 Gm.) may be necessary hypodermically to relieve colonic spasm.

2. Amebic dysentery or diarrhea with subacute onset and course is the ordinary type. Here the need for bed rest is proportioned to the severity of bowel disturbance. It is desirable to order the same diet as given under type 1 until symptoms are controlled, after which the dietary regimen should be the same as for chronic amebiasis. Drug treatment should be exactly as outlined under type 1 to the point of relief of symptoms, at which time the treatment should proceed as described for chronic amebiasis.

3. Chronic uncomplicated intestinal amebiasis, whether a simple so-called carrier state or a condition of recurrent or mildly persistent symptoms, is the most frequent type seen in this country. Either carbarsone or vioform are to be recommended. Carbarsone is given in gelatin capsules, each containing 0.25 Gm., two or three times daily to a total of twenty doses (5 Gm.). Much larger doses have been used with no evidence of toxicity.[29] The course may be repeated several times, intervals of at least ten days being allowed between the courses. The urine must show no evidence of renal irritation and the liver must be free from gross damage. These precautions are necessary with both of the drugs under consideration. Except for extensive colon ulceration and severe dysentery,

32. Faust, E. C.: Effect of Di-Hydranol on Intestinal Protozoa of Man and Laboratory Animals, Proc. Soc. Exper. Biol. & Med. **27**: 905 (June) 1930.

33. Anderson, H. H.; David, N. A., and Leake, C. D.: Oral Toxicity of Certain Alkyl Resorcinols in Guinea-Pigs and Rabbits, Proc. Soc. Exper. Biol. & Med. **28**: 609 (March) 1931.

34. James, W. M.: Some Observations on Intestinal Amebiasis Due to Infection with Endamoeba Histolytica, 16th Ann. Rep. Med. Dept., United Fruit Company, 1927, p. 185.

35. Anderson, H. H., and Reed, A. C.: Carbarsone Rectally in Amebiasis, Am. J. Trop. Med. **14**: 257 (May) 1934.

I have not found the rectal use of carbarsone necessary. Vioform may be given in 0.5 Gm. doses in gelatin capsules twice daily for ten days. If there is evidence of gastro-intestinal irritation, it can usually be avoided by having the capsules freshly coated with melted phenyl salicylate. This course can be repeated as needed, intervals of at least ten days being allowed. Vioform should not be given by rectum. In the small group of resistant cases, alternating courses of vioform and carbarsone may be used. Repetition of treatment should await reappearance of amebas in the stools.

The diet should in general have a high protein content, low roughage and low carbohydrates. Vitamins should be high, especially vitamin B.[36] Dunn,[37] writing from a large experience in Shanghai, says that "chronic amebic cases do well, not on a restricted diet, but on a diet rich in vitamins." Many others have also made this observation. Bed rest is not necessary. Bismuth subcarbonate, with or without dicalcium phosphate, frequently makes the patient more comfortable in diarrheic episodes, especially when secondary bacterial infection plays a part, as in type 5. Short courses of irrigations of 1:2,500 acriflavine hydrochloride, given each night for five or six nights, are often useful in relieving associated bacterial infection.

4. Extra-intestinal amebiasis presents an underlying pathologic condition essentially identical with that of intestinal lesions. For practical purposes, such conditions consist chiefly of hepatitis and liver abscess. Abscess of other organs and ulceration of the skin, especially contiguous with sinuses, may require some modification of local treatment. It is probable, a priori, that in every case of intestinal amebiasis the liver is invaded. But unless a frank hepatitis is present, or unless the pathologic process has advanced to the abscess stage, general treatment as already outlined is efficient to control it. In abscess or frank hepatitis, emetine is the drug of choice and should be administered as described under type 1. The subsequent treatment medicinally is the same as in chronic amebiasis. Local treatment of amebic abscess should consist of aspiration, repeated as needed, and irrigation with 1:2,500 solution of emetine hydrochloride. Cort[14] advises this procedure and states that if the fever disappears after emetine treatment it may be concluded that there is no secondary infection and therefore no need for open operation. In obscure cases, Cort advises the use of emetine as a therapeutic test.

5. Amebiasis may be complicated by other infections, by systemic diseases and by surgical conditions. In such cases the drug of choice must be selected with the entire clinical picture in view. For example, emetine would be used cautiously or not at all in the presence of myocarditis. Arsenicals would be used with caution in the presence of gross liver or kidney damage, optic nerve lesions and history of arsenical dermatitis.

With regard to complicating infections, it is to be remembered that bacillary dysentery may coexist and that the presence of some other disease of the bowel, such as cancer, may be masked by the amebic infection. There is reason to believe that amebic ulcerations of long standing may act as do other foci of infection, affording a portal of entry for bacteria, bacterial products and possibly also other chemical substances from the intestinal canal.

Surgical complications are not at all uncommon, especially in the wake of the recent Chicago outbreak. Proper treatment rests on early diagnosis, especially before or at the time of surgical intervention in the abdomen. Intensive emetine treatment is to be avoided before operation, because of the danger of weakening the myocardium. Careful diagnosis will often decide whether a moderate course, not to exceed 5 or 6 grains (0.3 or 0.36 Gm.) of emetine, should be given, or whether the emetine should begin immediately before or after the operation. Only good clinical judgment, with clear recognition of the possibilities of amebic lesions in the absence of discoverable amebas in the stools, will enable the physician to decide on wise therapy. But certainly he must have in mind the frequency with which amebic lesions simulate peptic ulcer, cholecystitis, perforation, appendicitis, gangrene and new growth, and also the extreme danger of operations involving the gastro-intestinal tract when amebic lesions are present and untreated. In this group of surgical complications, emetine is the drug of choice because of quickness of action, to be followed at the earliest safe moment by carbarsone. Surgical complications of amebiasis and amebic granulomas have been well discussed by Connor,[38] Gunn and Howard,[39] Gilman[40] and Hines.[41] It is to be remembered that surgical complications may appear early in a first acute attack or late in cases insufficiently treated; also that they may be discovered unsuspected at operation, or operation may be done without recognition or under a wrong or incomplete diagnosis. James[30] and others have advised "wide open cecostomy and thorough irrigations through the cecostomy and through the rectum as well . . . . It was found to be very effective in the acute fulminating types and also in the chronic types that did not yield to other treatment." Dudley Smith of San Francisco strongly advises a cecostomy, after the manner described by Phillips[42] of Los Angeles.

6. Sequels of amebiasis include sprue, chronic simple and chronic ulcerative colitis, cancer, chronic infections such as tuberculosis, residual ulceration and colitis maintained by secondary bacterial infection and mechanical disturbances such as scarring and stricture. These are to be considered separately by Dr. Lynch[43] and are noted here only for the sake of completeness. It is particularly to be noted that effective treatment early in the course of amebic infection is important in preventing such sequels.

7. The final clinical point needing attention from the point of view of treatment simply crystallizes what has been covered already in respect of the need of avoiding extra hazards from the drugs themselves. Anderson[44] has discussed this in detail. It is worthy of repetition that the best treatment will approach most nearly the following criteria: high clinical effectiveness, low toxicity, amenability to oral administration, noninterference with the usual activities of the patient, lack of need for adjuvant treatment, and low cost.

350 Post Street.

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Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY OF THE AMERICAN MEDICAL ASSOCIATION HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

H. A. CARTER, Secretary.

HANOVIA HOME MODEL ALPINE SUN LAMP ACCEPTABLE

This is a quartz mercury vapor arc lamp designed for prophylactic ultraviolet radiation applications and manufactured by the Hanovia Chemical and Manufacturing Company, Newark, N. J.

The Home Model Alpine Sunlamp is available in two forms, one for direct current, the other for alternating current. They operate on a 110 volt circuit.

The two lamps employ the same hemispherical polished aluminum hood and reflector mounted in such a way that the radiations may be projected downward or outward. The opening of the hood is 8½ inches in diameter, and at 36 inches the radiation covers a circular area about 30 inches in diameter.

The lamp comes either as a table model or as a stand type model. The stand type lamp is mounted on casters and is provided with vertical adjustment.

The electrical controls of the alternating current lamp are contained in a separate housing 9 by 7 by 8½ inches, weighing about 35 pounds. For the stand type lamp the electrical housing is mounted on the base. A double pole snap switch is provided on the lamp cord. The electrical circuit for the alternating current lamp consists of a transformer and reactor, with a small rheostat for line voltage adjustment, and ballast.

Hanovia Home Model Alpine Sun Lamp.

The light generator consists of a two electrode highly evacuated tubular vessel constructed entirely of fused quartz for direct current. This burner operates on either polarity. For alternating current a three electrode burner constructed entirely of fused quartz is employed. Both burners employ the fused-in wire seal.

The lamp is lighted by turning on the electric supply and tilting the burner for the establishment of the arc.

The Home Model Alpine Sun Lamp produces a characteristic quartz mercury arc spectrum with a spectral energy distribution closely resembling that previously given for the physician's therapeutic lamp, the Super Alpine Sun; however, since the electrical energy input is less, naturally the emitting radiation energy is less.

At a distance of 36 inches between the recipient with an average skin and the lamp, no more than fifteen minutes should be required to produce a perceptible erythema.

Suitable eye-protecting goggles must be worn when the Home Model Alpine Sun Lamp is employed.

Operating Characteristics

Alternating Current, 60 cycle (25 cycle requires special equipment)		Direct Current	
Line voltage	100 to 125 volts	Line voltage	100 to 125 volts
Starting amperage	5 amperes	Starting amperage	4 amperes
Operating amperage	2.9 amperes	Operating amperage	2 amperes
Wattage	300	Wattage	140
Burner voltage	135	Burner voltage	70
Burner wattage	200		

Note: The direct current lamp has two thirds the intensity of ultraviolet of the alternating current lamp.

Based on evidence that radiations from the mercury vapor arc in quartz lamps at the prescribed distance (36 inches) may prevent rickets and aid in the development of sound bones and teeth, the Council on Physical Therapy declares the Hanovia Home Model Alpine Sun Lamp acceptable for inclusion in its list of accepted devices for one year.

Committee on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COMMITTEE ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOLLOWING ANY NECESSARY CORRECTIONS OF THE LABELS AND ADVERTISING TO CONFORM TO THE RULES AND REGULATIONS. THESE PRODUCTS ARE APPROVED FOR ADVERTISING IN THE PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION, AND FOR GENERAL PROMULGATION TO THE PUBLIC. THEY WILL BE INCLUDED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION.

RAYMOND HERTWIG, Secretary.

(1) CEDAR HILL BRAND GOLDEN SYRUP
(2) CEDAR HILL BRAND WHITE SYRUP
(3) UNCLE SAM BRAND TABLE SYRUP
(4) PRESIDENT BRAND TABLE SYRUP

Distributors.—(1) and (2) Hassendeubel Grocery Company, St. Louis.

(3) and (4) Gildehaus, Wulfing & Co., St. Louis.

Packer.—Union Starch and Refining Company, Granite City, Ill.

Description.—(1) Table syrup; corn syrup flavored with refiners' syrup. The same as Golden Drip Brand Golden Table Syrup (THE JOURNAL, May 26, 1934, p. 1763).

(2) and (4) Table syrup; corn syrup sweetened with sucrose; flavored with vanilla. The same as Union Brand Crystal White Syrup (THE JOURNAL, Sep. 3, 1932, p. 833).

(3) Table syrup; corn syrup flavored with refiners' syrup. The same as Union Brand Golden Table Syrup (THE JOURNAL, July 23, 1932, p. 309).

GOOD MORNING PURE FLORIDA GRAPEFRUIT HEARTS

Distributor.—Chas. W. Bauermeister Company, Terre Haute, Ind.

Packer.—Dr. P. Phillips Company, Orlando, Fla.

Description.—Canned sliced Florida grapefruit sweetened with added sucrose and retaining in large measure the original natural vitamin content; the same as Dr. P. Phillips Florida Fanci-Cut Grapefruit Slices (THE JOURNAL, Nov. 19, 1932, p. 1781).

MONTCO STERILIZED EVAPORATED MILK

Distributor.—William Montgomery & Company, Philadelphia.

Packer.—The Defiance Milk Products Company, Defiance, Ohio.

Description.—Unsweetened, sterilized, evaporated milk. The same as Defiance Pure Evaporated Milk, THE JOURNAL, March 3, 1934, page 693.

FONTANA'S EGG NOODLES FINE
FONTANA'S EGG NOODLES WIDE
FONTANA'S EGG VERMICELLI FIDEOS

Manufacturer.—Fontana Food Products Co., San Francisco.

Description.—Noodles prepared from flour and egg yolk.

Manufacture.—The flour, egg yolks and water, in definite proportions, are mechanically mixed and kneaded. The resulting dough is rolled by machine to required thinness, cut, dried on racks under controlled conditions, and packed in cartons.

Analysis (submitted by manufacturer).—

	per cent
Moisture	12.4
Ash	0.6
Lipoids	5.7
Protein (N × 6.25)	13.0
Reducing sugars as dextrose	0.8
Sucrose	0.3
Crude fiber	0.2
Carbohydrates other than crude fiber (by difference)	68.1
Lipoid phosphoric acid as P_2O_5	0.13
Total phosphoric acid as P_2O_5	0.41

Calories.—3.8 per gram; 108 per ounce.

Claims of Manufacturer.—Complies with the United States Department of Agriculture definition and standard.

PHYSICIANS SPECIALIZING IN PATHOLOGY AND CLINICAL PATHOLOGY

PREPARED BY THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

For eight years the Council on Medical Education and Hospitals with the assistance of the committee of pathologists and of the local advisers has prepared lists of approved clinical laboratories and physicians specializing in pathology and clinical pathology. This work was begun by the Council in 1924 according to instructions received from the House of Delegates. In 1931 the listing of approved clinical laboratories as such was discontinued and a list of physicians specializing in pathology substituted. The laboratories supervised by the physicians listed may be said to be approved.

The original request for some regulation regarding clinical laboratories came from the clinical pathologists in 1923, the American Society of Clinical Pathologists and the American Association of Pathologists and Bacteriologists having worked independently for some time toward a solution of the problem. Some means of eliminating lay specialists in this field was sought. It was held improper for any person not qualified educationally and legally to assume the responsibility of making a diagnosis or prognosis, or of acting as a consultant with regard to disease in the human body. Where the law does not restrict diagnosis and the interpretation of laboratory observations to qualified medical practitioners, all other means available should be used to protect the patient against the incompetence of the lay specialist and the nonmedical clinical laboratory.

In order that patients may be given the benefit of the most accurate analysis with regard to source, nature and progress of disease, physicians should have their work carried out in laboratories under the supervision of capable pathologists. The progress made through the efforts of the Council, to distinguish medical from nonmedical laboratories and to determine which laboratories under medical supervision were to be relied upon, has been proportionate to the cooperation extended by the profession generally. Doubtless, this work has been responsible to some extent for the decrease in the use of lay-supervised clinical laboratories and has brought to many physicians an appreciation of the full importance of medical supervision over this work.

The present list of physicians specializing in pathology and clinical pathology contains 795 names. The first list published in 1926 contained the names of 162 laboratories. The list has grown at the rate of approximately 100 names per year. Physicians everywhere are urged through the publications of the Council to patronize only such laboratories as are under the direction of physician-pathologists, listed or eligible for listing. Applications for recognition on the approved list are being considered regularly by the Council and the local advisory committees.

In 1928 the Section on Radiology requested the Council to carry out a similar work for radiologists. A list of physicians specializing in radiology is also maintained by the Council in the same manner as the list for pathologists and clinical pathologists. At the present time, 1,270 radiologists have been admitted to the Council's list.

BIBLIOGRAPHY

The initial steps, beginning with the authorization of the movement by the House of Delegates of the American Medical Association at the annual session in San Francisco in 1923, are given in THE JOURNAL, April 3, 1926. That article contains the names of the members of the joint committee and gives a detailed account of the work of the committee and the Council on Medical Education and Hospitals during the years 1923, 1924 and 1925. It contains a copy of the original questionnaire and the compilation of statistics on clinical laboratories gathered from all states of the Union by means of that questionnaire. Of special importance are the principles stated by the joint committee at that time—important because most of them still hold good, yet some of them would hardly be regarded as pertinent at the present time. The first provisional list was published in the report just referred to. Subsequent developments in the evolution of the list, the present method of preparation and particularly the changes in the list itself, are reflected in the following references:

The second publication of the list appeared in THE JOURNAL, March 12, 1927, and contained 145 names; the list was next published in the Tenth Edition of the American Medical Directory in May 1927 and contained 145 names; in THE JOURNAL, March 24, 1928, 160 names; March 30, 1929, 174 names; in the Eleventh Edition of the American Medical Directory, July 1929, 175 names; in THE JOURNAL, March 29, 1930, 178 names; May 23, 1931, 183 names, and in the Twelfth Edition of the American Medical Directory, June 1931, 183 names; in THE JOURNAL, Oct. 22, 1932, 538 names; in THE JOURNAL, Oct. 14, 1933, 704 names.

The following list in this issue contains 795 names.

ESSENTIALS FOR THE LISTING OF PHYSICIANS SPECIALIZING IN PATHOLOGY AND CLINICAL PATHOLOGY

Admission to the list is open to all physician-pathologists engaged in pathologic work in accordance with the "Essentials," whether connected with a hospital or not. The work of compiling a list of qualified pathologists according to these "Essentials" is done by the Council on Medical Education and Hospitals of the American Medical Association, 535 North Dearborn Street, Chicago.

Definition.—A physician holding himself out as a specialist in pathology may be defined as follows: One who is a graduate in medicine having had satisfactory training and experience in pathology, chemistry, bacteriology or other allied subjects for at least three years subsequent to graduation, who is in good standing and has been duly licensed to practice medicine.

Qualifications.—(*a*) The pathologist shall be on a full or part time basis with a laboratory for the practical application of one or more of the fundamental sciences by the use of specialized apparatus, equipment and methods, for the purpose of ascertaining the pres-

ence, nature, source and progress of disease in the human body. He should devote the major part of his time to work in this field.

(*b*) Pathology should be practiced on the same scientific and ethical basis, whether in the hospital or in a detached laboratory. The work represents the practice of medicine as in other specialties.

The pathologist may make diagnoses only when he is a licensed graduate of medicine, has had satisfactory training and experience in pathology for at least three years subsequent to graduation from medical college, is reasonably familiar with the manifestations of disease, and is competent to make reliable reports.

(*c*) Assistant: The pathologist may have a corps of qualified assistants and technicians, responsible to him, and for whom he is responsible, to carry out promptly, intelligently and accurately the several kinds of service the laboratory offers. All their reports, not only of tissues but also of all bacteriologic, hematologic, biochemical, serologic and pathologic data, should be made to the pathologist.

Scope.—A general pathologic laboratory should be prepared to render the following services:

(*a*) Hematologic: Blood counts, blood groupings and coagulation tests, and tests for blood parasites in general.

(*b*) Biochemical: Qualitative and quantitative analyses of urine, blood, gastric contents, body fluids, feces, intestinal contents and cerebrospinal fluids; renal and hepatic function tests and basal metabolism.

(*c*) Bacteriologic: Bacteriologic diagnoses; preparation of vaccines and blood and body fluid cultures.

(*d*) Serologic: Serologic diagnoses; agglutination, complement fixation, or precipitin and lysis tests.

(*e*) Pathologic: Preparation of paraffin, celloidin or frozen sections, microscopic and gross pathologic specimens and necropsies.

(*f*) Parasitologic: Protozoal and zoological diagnoses.

(*g*) Metabolic: Disorders of metabolism.

(*h*) Cardiologic: Disorders of the heart.

It is of course not expected that the candidate shall be prepared to render all the services mentioned, since the work must necessarily be diversified in larger laboratories and in smaller laboratories it is not always practical to have equipment and setups that would be used only occasionally. Since many pathologists limit their work to one branch of the specialty, referring certain items, far more efficiency is to be expected.

Reports.—Reports should be made solely to the physician in charge of the patient and should be signed by the pathologist. All blanks and reports should have the name of the director printed on them and, if of a diagnostic or prognostic character, the name of the staff physician also.

Records.—Full records of all examinations made by the pathologist, suitably indexed and filed, are essential. Every specimen analyzed in the laboratory should be given a serial number, which should follow that specimen in the records and reports. When the laboratory report concerns a hospital patient, an exact transcript of the laboratory record should be appended to the hospital case record. Each specimen submitted to the laboratory should be accompanied by pertinent clinical data.

Library.—The laboratory should be provided with, or have convenient access to, a library including current scientific books and journals on all the various subjects required in its work.

Fees.—There should be no dividing of fees or rebating between the laboratory or its pathologist and any physician, corporate body or group.

Publicity.—Publicity should be in professional good taste and be limited to statements of fact, as the name, address and telephone number of the laboratory; names and titles of the pathologist and other active responsible personnel; fields of work covered; office hours; directions for sending specimens, and the like, and should not contain misleading statements or claims of unusual superiority. It should not advocate medical fads nor lay undue stress on the importance of laboratory observations.

Only the names of those rendering regular service to the laboratory should appear on letterheads, or any other form of publicity, as being connected with the laboratory.

Advertising matter should be directed only to physicians either through bulletins or through recognized technical journals, and never to the nonprofessional public, as, for example, by announcements in popular journals and periodicals, circulars, pamphlets, telephone lists or other means.

PHYSICIANS SPECIALIZING IN PATHOLOGY AND CLINICAL PATHOLOGY

The following list contains the names of 795 physicians specializing in pathology, laboratory diagnosis or clinical pathology, who returned the questionnaire, who were found to meet the "Essentials" and were recommended by the Council's advisers. Those engaged in teaching, research and other activities are admitted, as well as those in active practice. For the list of physicians specializing in pathology in government service, see page 1235.

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Weingart, Julius S.....406, 6th Ave.

Dubuque
McNamara, Frank P.....1596 Delhi St.

Iowa City
Herrmann, Walter W.....University of Iowa

Ottumwa
Hecker, Friedrich A.....130 E. Maple Ave.

Sioux City
Starry, Allen C.....21st and Court Sts.

KANSAS

Kansas City
Wahl, Harry R...39th St. and Rainbow Blvd.

Salina
Moses, Howard N.....100 S. Santa Fe St.

Topeka
Lattimore, John L.....901 Kansas Ave.

Wichita
Hellwig, C. Alexander....928 N. Emporia Ave.

KENTUCKY

Lexington
Maxwell, Elmer S.....190 N. Upper St.

Louisville
Allen, John D.....608 S. 4th St.
McNeill, Clyde.....321 W. Broadway
Miller, Aura J.....323 E. Chestnut St.
Weeter, Harry M.....332 W. Broadway

LOUISIANA

Baton Rouge
Beven, John L.....
.....Our Lady of the Lake Sanitarium

Lake Charles
Hebert, Louis A.....834 Ryan St.

Monroe
Pracher, John.....301 Jackson St.

New Orleans
Friedrichs, Andrew V.....921 Canal St.
Johns, Foster M.....927 Canal St.
Lanford, John A.....3516 Prytania St.
Lawson, Edwin H.....2700 Napoleon Ave.
Maher, Aldea.....228 St. Charles St.

Shreveport
Butler, Willis P.....940 Margaret Pl.
Ellis, Fredk. G.....624 Travis St.

MAINE

Bangor
Thompson, H. E.....250 State St.

Lewiston
Belliveau, Romeo A.....89 Pine St.
Gottlieb, Julius.....49 Central Ave.

Portland
Warren, Mortimer.....22 Arsenal St.

MARYLAND

Baltimore
Collenberg, Henry T.....2 W. Read St.
Gichner, Manuel G.....2426 Eutaw Pl.
Maldeis, Howard J.....104 W. Madison St.
Spencer, Hugh R.....University of Maryland

MASSACHUSETTS

Boston
Belding, David L.....80 E. Concord St.
Branch, Chas. F.....80 E. Concord St.
Burnett, Francis L.....205 Beacon St.
Flashman, David H.....37 Schuyler St.
Hinton, Wm. A.....25 Bennet St.
Hooker, Sanford B.....80 E. Concord St.
Leary, Olga Cushing.....43 Bay State Rd.
Leary, Timothy.....43 Bay State Rd.
Mallory, Tracy B.....
.....Massachusetts General Hospital
Oslin, J. Edwin.....30 Huntington Ave.
Rooney, James Stewart....53 Parker Hill Ave.
Schlesinger, Monroe J....330 Brookline Ave.
Steele, Albert E.....475 Commonwealth Ave.
Ulrich, Helmuth.....30 Huntington Ave.
Warren, Shields.....195 Pilgrim Rd.

Bradford
Bartlett, Bernice A.....11 Haseltine St.

NAME — ADDRESS

Brookline
Dalrymple, S. C.....233 Walnut St.

Fall River
Peasley, Elmus D.....1820 Highland Ave
Walsh, James H.....538 Prospect St.

New Bedford
Wason, Isabel Mary.....146 Cottage St.

Pittsfield
Criscitiello, Modestino.....8 Bank Row

Springfield
Dwyer, John E.....146 Chestnut St.

Westboro
Pierce, Lydia Baker.....

Worcester
Elliott, William J.....119 Belmont St.
Freeman, William.....P.O. Box 489
Goodale, Raymond H.....71 Jacques Ave.
Looney, Joseph M....Worcester State Hospital

MICHIGAN

Ann Arbor
Bugher, John C..Dept. of Path., Univ. of Mich.
Gordon, Harold...Dept. of Path., Univ. of Mich.
Howard, S. C.....326 N. Ingalls St.
Wanstrom, Ruth C.....
.....Dept. of Path., Univ. of Mich.
Weller, C. V...Dept. of Path., Univ. of Mich.

Battle Creek
Lewis, Welcome B....Battle Creek Sanitarium
Roth, Paul.....Battle Creek Sanitarium

Bay City
Gamble, Wm. G., Jr.....2010, 5th Ave.

Detroit
Amolsch, Arthur L.Wayne Univ., Coll. of Med.
Brines, Osborne A.....
.....Macomb and St. Antoine Sts.
Clark, Harry L.....5057 Woodward Ave.
Cope, Henry E.....1551 Woodward Ave.
Davis, James E.....1512 St. Antoine St.
Hartman, Frank W.....2799 W. Grand Blvd.
Kasper, Jos. A.....1151 Taylor Ave.
Morse, Plinn F.....3825 Brush St.
Oginsky, M. A.....226 Hancock Ave., E.
Owen, Clarence I.....4160 John R St.
Owen, R. G.....1551 Woodward Ave.
Stafford, Frank W.....1111 Griswold St.

Flint
Backus, Glenn R.....901 Begole St.

Grand Rapids
Bond, Geo. L.....74 Ionia Ave., N. W.
German, Wm. M...Blodgett Memorial Hospital

Grosse Pointe
Gruhzit, Oswald M.....580 Hampton Rd.
King, Walter E.....704 Lincoln Rd.

Kalamazoo
Prentice, Hazel R.....3404 Oakland Dr.

Saginaw
Lohr, Oliver W.....302 S. Jefferson St.

MINNESOTA

Duluth
Berdez, George Louis.....St. Mary's Hospital

Minneapolis
Baker, Looe.....1111 Nicollet Ave.
Dahlstrom, Arthur Wm.....91 S. 7th St.
Drake, Charles R.....900 Nicollet Ave
Grave, Floyd.....823 Nicollet Ave.
Lufkin, Nathaniel H.....
.....424 W. Diamond Lake Rd.
Merkert, Geo. L.....1412 E. 24th St.
Smith, Margaret I.....2627 Chicago Ave.

Rochester
Beaver, Donald C.....Mayo Clinic
Broders, A. C.....Mayo Clinic
Kernohan, J. W.....Mayo Clinic
MacCarty, Wm. C.....Mayo Clinic
Magath, Thos. B.....Mayo Clinic
Robertson, H. E.....Mayo Clinic
Rosenow, E. C.....Mayo Clinic
Sanford, Arthur H.....Mayo Clinic
Wellbrock, Wm. L. A.....Mayo Clinic
Wilson, Louis B.....Mayo Foundation

St. Cloud
Stangl, Fred H.....101 7th Ave., S.

St. Paul
Ikeda, Kano.....123 W. College Ave.
Noble, John Franklin.....Ancker Hospital

MISSISSIPPI

Greenville
White, E. T.....301½ Washington Ave.

Meridian
Krauss, William.....1521, 24th Ave.

Vicksburg
Lippincott, Leon S.....920 Crawford St.

MISSOURI

Columbia
Neal, M. Pinson..Dept. of Path., Univ. of Mo.
Pfaum, Clarence C.....
.....Dept. of Path., Univ. of Mo.

Jefferson City
Adams, Charles F...Mo. State Board of Health

Kansas City
Duncan, Ralph Emerson.....306 E. 12th St.
Hall, Frank J.....306 E. 12th St.
Helwig, Ferdinand C.....St. Luke's Hospital
Johnson, Emsley T.....St. Joseph Hospital
Koritschoner, Robt.....4949 Rockhill Rd.
Narr, Frederick C.....Research Hospital
Stewart, Edward L.....1115 Grand Ave.
Trimble, Wm. K.....1103 Grand Ave.

St. Louis
Allen, Hollis N.....634 N. Grand Blvd.
Buhman, Rudolph.....539 N. Grand Blvd.
Gradwohl, R. B. H.....3514 Lucas Ave.
Harris, D. L.....508 N. Grand Blvd.
Ives, Geo.....3720 Washington Blvd.
Katz, Samuel D.....3720 Washington Blvd.
Klenk, Chas. L.....508 N. Grand Blvd.
McCordock, Howard A.....Washington Univ.
Schery, Chas. Wm.....529 N. Whittier St.
Siebert, Walter J.....Washington Univ.
Thompson, Ralph L.....607 N. Grand Blvd.
Walsh, L. S. Newman.....5535 Delmar Blvd.

Springfield
Stone, Murray C.....200 E. Pershing St.

University City
Thurston, Eric W.....6651 Enright Ave.

MONTANA

Butte
Peterson, Raymond F.....57 W. Quartz St.

Great Falls
Hitchcock, E. D.....Great Falls Clinic
Walker, Thos. F.....563, 1st Ave., N.

NEBRASKA

Omaha
Eggers, Harold E.Univ. of Nebr., Coll. of Med.
Manning, E. T.....107 S. 17th St.
Moody, W. B.....206 S. 19th St.
Myers, John T....Univ. of Nebr., Coll. of Med.
Rubnitz, A. S.....107 S. 17th St.
Russum, B. Carl.....306 N. 14th St.
Tollman, James P.....42nd and Dewey Ave.

NEVADA

Reno
Parsons, Lawrence.....235 W. 6th St.

NEW HAMPSHIRE

Hanover
Miller, Ralph E.....9 Downing Rd.

NEW JERSEY

Arlington
Gilman, C. M. B.....59 Seeley Ave.

Asbury Park
de Pons, Isabel S. C.....501 Grand Ave.
Pons, C. A.....501 Grand Ave.

Atlantic City
Kilduffe, Robt. A.....26 S. Ohio Ave.

Bayonne
Antopol, Wm.....Bayonne Hospital

Elizabeth
Casilli, A. R.....618 Newark Ave.

Englewood
Halpern, Herman.....143 Engle St.

Greystone Park
Christian, Thos. B.....

Jersey City
Alter, Nicholas M.....410 Fairmount Ave.

Mount Holly
Viteri, Luis E.....137 High St.

Newark
Brown, Lewis W.....15 Fulton St.
Echikson, Joseph I.....845 S. 12th St.
Goldberg, Samuel A.....27 S. 9th St.
Gray, John W.....142 Clinton Ave
Yaguda, Asher.....201 Lyons Ave.

Orange
Cline, Benj. F.....264 Central Ave.

Paterson
Davis, A. Hobson.....528 Market St.
Kim, Gay B.....703 Main St.

Plainfield
Borow, Louis S.....934 Park Ave.

Teaneck
Markley, Luther A.....Holy Name Hospital

Toms River
Halbach, Robert McC.....513 Main St.

Trenton
Rogers, Wm. N.....1255 Brunswick Ave.

NEW MEXICO

Albuquerque
Beam, M. P.....221 W. Central Ave.

NEW YORK

Albany
Gilbert, Ruth.....116 N. Allen St.
Horner, Henrietta Calhoun..171 S. Main Ave.
Jacobsen, V. C.....44 Lawnridge Ave.
Klinck, Gustavus H., Jr.....Albany Med. Coll.
Wright, A. W.....Albany Med. Coll.

Binghamton
Bergstrom, V. W.....21 Park Ave.
Gregory, Hugh S.....Binghamton State Hosp.

Brooklyn
Black, F. A.....32 Court St.
Derby, Irving Marsh.....681 Clarkson Ave.
Fein, M. J.....50 Greene Ave.
Fink, Harold.....1304 Beverly Rd.
Grainick, Abraham.....119 Sumner Ave.
Greeley, Horace.....140 Clinton St.
Kantrowitz, Abraham R.....475 Ocean Ave.
Lederer, Max.....555 Prospect Pl.
Marten, M. Edward.....515 Ocean Ave.
McNally, Robert F.....1010 Bushwick Ave.
Miller, Margaret A.....437 Ovington Ave.
Moitrier, Wm., Jr.....1219 Dean St.
Morrison, Maurice.....250 Ocean Pkwy.
Nidish, Edward H.....1272 Bergen St.
Polayes, Silik H.....425 Prospect Pl.
Wiener, Alexander S.....520 Crown St.

Buffalo
Bentz, Charles A....126 W. Humboldt Pkwy.
Hanan, Ernest B.....462 Grider St.
Jacobs, William F.....408 Richmond Ave.
Vaughan, Stuart L.....100 High St.
Warwick, Margaret.....875 Lafayette Ave.
Williams, Herbert U.....30 Arlington Pl.

Central Islip
Trygstad, Reidar.....Central Islip State Hosp.

Clifton Springs
Thomas, Walter S.....42 Kendall St.

Corning
Shafer, Rudolph J.....163 E. 1st St.

Cortland
Wall, Wm. A.....134 Homer Ave.

Elmira
Bleyer, Leo F.....555 E. Market St.
Stuart, Anna M.....656 Park Pl.

Far Rockaway
Handelman-Kalashnikoff, Pauline.....
.....536 Beach 22d St.

Glens Falls
Maslon, Morris.....191 Glen St.

Ithaca
Hauenstein, B. F.....
.....Tompkins Co. Memorial Hospital

Jamaica
Buxbaum, Edward J.....8711, 150th St.
Campbell, N. H. M.....89-18, 139th St.
Werne, Jacob.....89-04, 148th St.

Kings Park
Priestman, Gordon.....

Little Neck
Van Nostrand, Hobart S.....
..... 45-06 Little Neck Pkwy.

Long Island City
Angrist, Alfred.....43-42, 45th St.
Hala, Wm. W.....30-20, 29th St.

Marcy
Bower, George C.....Marcy State Hospital

Middletown
Kelly, Wm. F.....
.....Middletown State Homeopathic Hosp.

Newark
Baumgartner, E. A.....Newark State School

Newburgh
Wescott, A. M.....231 Liberty St.

New Rochelle
Brooks, Henry T.....35 Woodland Ave.
McIlroy, P. T.....421 Huguenot St.

New York
Aronson, Wm.....150 E. 182d St.
Brown, Chester R.....150 W. 87th St.
Cocheu, Lindsley F.....205 E. 69th St.
Curphey, Theodore J.....115 E. 61st St.
Darlington, Charles G.....75 E. 55th St.
Dolgopol, Vera B.....131 W. 110th St.
Donnet, J. Victor.....152 W. 58th St.
DuBois, Phebe L.....150 E. 73d St.
Eggston, Andrew A.....653 Park Ave.
Ehrlich, Joseph C.....220 Boscobel Pl.
Elser, Wm. J.....525 E. 68th St.
Ewing, James.....2 W. 106th St.
Felsen, Joseph.....667 Madison Ave.
Ferraro, Louis R.....711 E. 230th St.
Foot, Nathan Chandler.....525 E. 68th St.
Fraser, Alexander.....153 W. 11th St.
Frosch, Herman L.....1882 Grand Concourse
Geiger, Jacob.....25 Central Park West
Gonzales, Thomas A.....56 E. 87th St.
Grauer, Frank.....226 W. 71st St.
Hadjopoulos, L. G.....6 E. 78th St.

NAME — ADDRESS

Heitzmann, Louis....38 W. 90th St.
Helpern, Milton....155 E. 91st St.
Hillman, Oliver S....140 E. 54th St.
Hochman, Charles H...2715 Grand Concourse
Jacobson, Sheldon A....1919 Madison Ave.
Jaffe, Henry L....1919 Madison Ave.
Jeffries, Ferdinand M....18 E. 41st St.
Jessup, D. S. D....411 W. 114th St.
Kaliski, David J....70 E. 83d St.
Klemperer, Paul....385 Central Park West
Kopel, Moses....1454 Grand Concourse
Larimore, L. D....750 Riverside Dr.
Lisa, James R....New York City Hospital
MacNeal, W. J....303 E. 20th St.
Manheims, Perry J....27 W. 96th St.
McNeil, Archibald....18 E. 41st St.
Moolten, Sylvan E....60 E. 96th St.
Olcott, Charles T....1300 York Ave.
Pincus, Julius....250 W. 75th St.
Price, Aaron S....335 W. 50th St.
Rohdenburg, G. L....111 E. 76th St.
Rosenthal, Nathan....51 E. 90th St.
Rous, Peyton....
..Rockefeller Institute for Medical Research
Rubinstein, Morris....600 W. 181st St.
Saccone, Andrea....334 E. 116th St.
St. George, Armin....400 E. 29th St.
Seecof, David P....1970 Daly Ave.
Shuster, Mitchell....30 E. 40th St.
Smith, Lawrence W..Willard Parker Hospital
Sondern, Frederic E....20 W. 55th St.
Sophian, L. H....428 W. 59th St.
Stanford, Addie D....450 E. 64th St.
Stillman, Ralph G....525 E. 68th St.
Taub, Jacob....1574 Leland Ave.
Thro, William C....1300 York Ave.
Weiss, M. Arthur....235 W. 76th St.
Whitcher, Burr R....305 E. 20th St.

Ossining
Gosline, Harold I....275 Spring St.

Ozone Park
DeVeer, J. Arnold....101-32 97th St.

Poughkeepsie
Carpenter, H. P...Hudson River State Hospital
Peckham, A. L....Vassar Brothers Hosp.

Rochester
Brown, Herbert R....224 Alexander St.
Gáspár, István....501 W. Main St.
Hawkins, William B....260 Crittenden Blvd.
Kennedy, Robert P....176 S. Goodman St.
Lindsay, Saml. T....909 W. Main St.
O'Grady, Geo. W....277 Alexander St.

Rye
Loder, M. M....

Saranac Lake
Gardner, L. U....7 Church St.

Schenectady
Kellert, Ellis....Ellis Hospital

Syracuse
Ferguson, J. Howard....309 S. McBride St.
Weiskotten, H. G....309 S. McBride St.

Troy
Curry, A. Hazel....467 Pawling Ave.
Curtis, Stephen H....41, 114th St.

Utica
Gallagher, C. D....1676 Sunset Ave.
Russell, Clarence L....1125 Court St.

Valhalla
Dalldorf, Gilbert J....Grasslands Hospital
Russell, Hollis K....Grasslands Hospital
Springer, Joyce M....Grasslands Hospital

Watertown
Walker, Thomas T....832 Washington St.

Westfield
Field, Cyrus W....88 N. Portage St.

Yonkers
Cook, Ward H....Dept. of Public Health

NORTH CAROLINA

Asheville
Crump, Curtis.... 36 Grove St.

Chapel Hill
Bullitt, James B....

Charlotte
Barret, Harvey P....403 N. Tryon St.
Todd, Lester C....403 N. Tryon St.

Durham
Baker, Roger D....Duke Hospital
Byrnes, Thomas H....Watts Hospital
Forbus, Wiley D....Duke Hospital
Porro, Francis W....Duke Hospital
Rigdon, Raymond H....Duke Hospital
Sprunt, Douglas H....Duke Hospital

Wake Forest
Carpenter, C. C...Wake Forest School of Med.

Wilmington
Barefoot, Graham B....1605 Grace St.

NORTH DAKOTA

Bismarck
Larson, L. W....221, 5th St.

Grand Forks
Saiki, A. K....Univ. of N. Dak. Med. Sch.

OHIO

Akron
Potter, Frederick C....256 W. Cedar St.
Saylor, Edward L....525 E. Market St.

Cincinnati
Faller, Albert....19 W. 7th St.
Herzberg, Mortimer....3261 Burnet Ave.
Patterson, James N....Univ. of Cincinnati
Zeek, Pearl M...Burnet Ave. and Goodman St.

Cleveland
Dominguez, Rafael....2272 S. Taylor Rd.
Karsner, Howard T....2085 Adelbert Rd.
Kline, Benjamin S....1800 E. 105th St.
Moritz, Alan R....2085 Adelbert Rd.

Columbus
Coons, J. J....370 E. Town St.
Fidler, Roswell S....700 N. Park St.
Hoffman, Ralph W....1542 W. 1st Ave.
Reinhart, Harry L....1711 Essex Rd.
Shilling, Ellis Ray....345 E. State St.

Dayton
Payne, Foy C....201 S. Main St.
Simpson, Walter M....134 Apple St.

Dover
Shaweker, Max....Reeves Bank Bldg.

Elyria
Rosenzweig, Maurice....630 E. River St.

Lorain
Donaldson, John B....700 Broadway

Toledo
Crumrine, Ralph M....
....Lucas County General Hospital
Hindman, S. S....316 Michigan St.
Ramsey, Thomas L....225 Michigan St.
Rucker, James B., Jr....630 W. Central Ave
Schade, August H....320 Michigan St.
Steinberg, Bernhard....Toledo Hospital
Zbinden, Theodore....706 Madison Ave.

Youngstown
Kramer, G. B....Youngstown Hospital

OKLAHOMA

Bartlesville
Chamberlin, E. M....329 S. Johnstone Ave.

El Reno
Muzzy, Wm. J....212 S. Evans St.

Oklahoma City
Bailey, Wm. H....300 W. 12th St.
Jeter, Hugh G....1200 N. Walker St.

Tulsa
Nelson, I. A....108 W. 6th St.
Venable, Sidney C....420 S. Main St.

OREGON

Eugene
Furrer, Emil D....130 E. Broadway

Portland
Foskett, H. H....1058 S. W. Taylor St
Hunter, Warren C..Univ. of Oregon Med. Sch.
Lawrence, H. J....322 Alder St.
Manlove, Chas. H...2266 Marshall St., N. W.
Menne, Frank R...Univ. of Oregon Med. Sch.
Robertson, Thomas D....2545 N. E. 45th St.

PENNSYLVANIA

Abington
Elman, John....York and Woodland Rds.

Allentown
Milstead, L. C....4th and Chew Sts.
Wenner, John J....941 Hamilton St.
Williams, Helen L...Allentown State Hospital

Altoona
Brumbaugh, A. S....1312, 11th St.

Ardmore
Belk, William P....Times Med. Bldg.

Chester
Sickel, Geo. B....525 Welsh St.

Danville
Hunt, Henry F....

Easton
Gaines, Carl....130 N. 3d St.
Zillessen, F. O....244 Bushkill St.

Erie
Armstrong, E. L....2d and State Sts.

Gettysburg
Stewart, Henry....

Greensburg
Mayhew, J. Morgan....532 W. Pittsburgh St.

Harrisburg
Denison, Charles M..Harrisburg State Hospital
Moffitt, George R....Harrisburg Hospital
Van Horn, Herman H....
....3d St. and Polyclinic Ave.

Huntingdon
Reiners, Charles R....741 Washington St.

Johnstown
Anderson, Horace B....218 Franklin St.
McCloskey, B. J....1020 Franklin St.

Kingston
Daley, D. F....214 Chestnut St.
Wenner, Thos. J....562 Wyoming Ave.

Lancaster
Keasbey, Louisa A....323 W. King St.

Lansdowne
Kennedy, Patrick J....65 Fairview Ave.

McKeesport
Sandblad, A. G....1701 Union St.

New Brighton
McLaren, Harold J....541, 11th Ave.

Norristown
Laubach, Charles A..Norristown State Hospital
Simpson, John C....920 Swede St.

Philadelphia
Asnis, Eugene J....1524 Chestnut St.
Barthmaier, O. F....2303 W. Lehigh Ave.
Bauer, John T....8th and Spruce Sts.
Beck, James S. P...Univ. of Pa., Sch. of Med.
Becker, Carl Emil....2341 N. College Ave.
Brown, Claude P. ....1930 Chestnut St.
Bucher, Carl Joseph....15th and Spruce Sts.
Case, Eugene Allen....1818 Lombard St.
Clark, J. H....3701 N. Broad St.
Corson-White, E. P....1820 Pine St.
Crawford, Baxter L....
....Jefferson Med. Coll. and Hosp.
de Rivas, Damaso....1831 Chestnut St.
Fanz, John I....Temple Univ. Sch. of Med.
Fowler, Kenneth....Presbyterian Hospital
Fox, Herbert..Pepper Laboratory, Univ of Pa.
Gault, Edwin S....Temple Univ. Sch. of Med.
Ginsburg, Gershon....1936 N. 7th St.
Hastings, W. S....Hasbrook and Hartel Sts.
Hopp, George A....20th and Chestnut Sts.
Konzelmann, F. W....Broad and Ontario Sts.
Krumbhaar, E. B...Univ. of Pa. Sch. of Med.
Long, Esmond R....Henry Phipps Institute
Lucké, Balduin...University of Pennsylvania
Lynch, Frank B., Jr....
....Germantown Disp. and Hosp.
McFarland, Joseph....
....McManes Laboratory, Univ. of Pa.
Meranze, David R....1429 S. 5th St.
Moon, V. H..Jefferson Med. Coll. and Hospital
Rees, William T....3763 N. 18th St.
Reimann, S. P....Lankenau Hospital
Richardson, Russell....320 S. 16th St.
Rose, S. Brandt....4035 Chestnut St.
St. John, E. Quintard....1833 Chestnut St.
Spaeth, William L. C....5000 Jackson St.
Stewart, Harold L....
....Jefferson Med. Coll. and Hospital
Tuft, Louis....1530 Locust St.

Pittsburgh
Baker, Moses H....121 University Pl.
Bruecken, A. J....St. Francis Hospital
Cohen, Mortimer....
....Univ. of Pittsburgh Med. Sch.
Grauer, Robert C....2001 Murray Ave.
Hamilton, Robt. C....Reed and Roberts Sts.
Haythorn, Samuel R..210 E. Park Way, N. S.
Joyce, Francis W....4001 California Ave.
Lacy, George Rufus....
....Univ. of Pittsburgh Med. Sch.
McClellan, Robt. H....265, 46th St.
Mellon, Ralph R....6055 Bunkerhill Dr.
Moyer, Ray P....1021 Portland St.
Permar, Howard H....Pride and Locust Sts.
Ray, Henry M....500 Penn Ave.
Rockman, Jacob....2117 Carson St.
Ross, Elizabeth....5230 Centre Ave.
Semsroth, Kurt....4800 Friendship Ave.
Wallhauser, Andrew....220 Shady Ave.
Willetts, Ernest W....429 Penn Ave.
Yardumian, K....Montefiore Hospital

Pottsville
Moll, Francis K....309 Manhantongo St.

Reading
Elton, Norman W....2008 Steuben Rd.
Funk, Erwin Deaterly....Reading Hospital

Sayre
DeWan, Chas. H....

Scranton
Clark, Geo. A....129 Washington Ave.
Cooper, Harold B....633 E. Market St.

Sewickley
Feltwell, Myrtle R....

Sharon
Hartman, Geo. O....740 E. State St.

Torrance
Wiseman, John Ignatius....

Warren
Eaton, H. C....Warren State Hospital

West Chester
Hollingsworth, I. P. P....411 N. Walnut St.

Wilkes-Barre
Janjigian, R. R....River and Auburn Sts.

York
Jamieson, Howard M....
....S. George St. and Rathton Rd.

NAME — ADDRESS

RHODE ISLAND

Howard
Crank, Rawser P. ..... State Hospital for Mental Diseases

Providence
Clarke, B. Earl ..... 593 Eddy St.
Hamilton, James ..... 349 Hope St.
Schradieck, C. E. ..... 825 Chalkstone Ave.

SOUTH CAROLINA

Charleston
Johnson, Francis B. ..... 16 Lucas St.
Lynch, Kenneth M. ..... 6 Lucas St.

Columbia
Plowden, Henry H. ..... 2020 Hampton St.
Smith, Herbert M. ..... State Office Bldg.

Greenville
Wilson, Thos. R. W. ..... 109 Memminger St.

Spartanburg
Mosteller, Ralph ..... 855 N. Church St.

SOUTH DAKOTA

Vermillion
Ohlmacher, Joseph C. ..... 309 Lewis St.

TENNESSEE

Chattanooga
Ball, Robert P. ..... 921 E. 3d St.
Crowell, Tolbert C. ..... 544 McCallie Ave.

Knoxville
DePue, Ray V. ..... 601 Walnut St.
Monger, Ralph H. ..... 603 W. Main Ave.

Memphis
Leake, Nolan E. ..... 899 Madison Ave.
McIntosh, J. A. Jr. ..... 264 Jackson Ave.
Moss, Thomas C. ..... 1265 Union Ave.
Schmittou, L. V. ..... 130 Madison Ave.

Nashville
Jones, Robt. L. ..... 706 Church St.

TEXAS

Austin
Bohls, Sidney W ..... 410 E. 5th St.
Graham, Geo. M. ..... 110 W. 7th St.
Jackson, J. Warren ..... 110 W. 7th St.

Beaumont
Lewis, Seaborn J. ..... 398 Pearl St.
Williford, H. B. ..... 595 Orleans St.

Dallas
Bell, Marvin D. ..... 1719 Pacific Ave.
Black J. Harvey ..... 1719 Pacific Ave.
Brandes, W. W. ..... 3301 Junius St.
Caldwell, Geo. T. ..... Baylor Univ. Coll. of Med.
Carter, Chas. F. ..... 1719 Pacific Ave.
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SATURDAY, OCTOBER 20, 1934

THE TREATMENT OF MUSCULAR DYSTROPHY WITH GLYCINE

The idea of treating muscular dystrophy by the administration of glycine resulted directly from chemical analysis of the urine. The fact that the method is not yet definitely established as clinically successful in the present form of application does not detract from the essential importance of the fundamental observations. Creatinuria has been noted in many diseases that primarily or secondarily attack the muscular system. This led Thomas and his co-workers to investigate the effect of prolonged administration of glycine on the clinical course of progressive muscular dystrophies. In their preliminary report it was stated that the ingestion of from 15 to 20 Gm. of glycine daily raised the creatinuria of different cases by different degrees, depending on the extent of the original creatinuria. After some weeks the creatinurias were found to decrease despite the continuance of glycine. Coincident with the decrease in the creatinuria there was a rise in the creatinine output and an improvement in the patient's ability to hold ingested creatine. It was also reported that simultaneously the patients improved clinically.

Cuthbertson and Maclachlan [1] recently reported the results of prolonged glycine administration in nine cases of muscular dystrophy of different types and in two other cases exhibiting selective muscular atrophy. The conditions of observation were controlled as carefully as possible. There was no massage, and no electrical or tonic treatment was given, but the patients were allowed to be up and encouraged to exercise according to their powers. They were placed on a basal diet free from meat, meat extract and fish. The total creatinine and preformed creatinine outputs were estimated in the twenty-four hour specimens of urine. The difference between the two estimations represented the quantity of creatinine excreted. At various intervals the patients' reaction to ingested creatine was determined. During these periods no glycine was taken. The amounts excreted were expressed as milligrams of nitrogen daily. Glycine therapy was usually started about three or four days after the first dose of creatine. The adults received 15 Gm. daily, the children 10 Gm. daily, dissolved in milk. Generally speaking, the greater the muscular incapacity the greater the degree of creatinuria and the less the excretion of creatinine.

In testing the reaction to the ingestion of creatine, 4.4 Gm. of anhydrous creatine was taken in one dose by the adults and 2.64 Gm. by the children. In the cases of muscular dystrophy the initial retentions of ingested creatine varied from 41 to 60 per cent of the intake in adults and from 42 to 78 per cent in the children. In the two cases of muscular atrophy the percentage retentions were 59 and 44. Following glycine therapy a definite increased retention capacity was noted in only one case of dystrophy. Four showed definitely diminished retention capacities. In three there was a definite coincident increase in the creatinine excretion. Following the ingestion of glycine, the creatine excretions increased in all the cases of dystrophy, in some to three or four times their basal values. These maximum periods of creatine excretion occurred during the first three weeks of therapy. The maximum daily creatine excretions in the various cases did not always occur in the period of maximum excretion, though this was usually the case. Following these periods of maximum excretion the daily excretions of creatine generally fell in some instances to below the basal level. Subsequent readministration of glycine after an intermission was usually accompanied by an increased creatinuria.

Clinically, five of the nine cases of muscular dystrophy were of the pseudohypertrophic type. With one exception the cases belonging to the dystrophy group showed definite general improvement as evidenced by increase in weight, gain in strength and feeling of well being. None of the patients became worse. In the majority there was also some evidence of improvement in the power of some of the specific muscles affected, but this was least in the pseudohypertrophic group. The Glasgow workers believe that in the majority of the cases the changes were in excess of those which might be expected to occur from hospitalization alone but that the term "cure" cannot be applied to the end results.

In another investigation on the same subject, the Linnewehs [2] attempted to study the question of possible glycine deficiency in muscular dystrophy. Their work was based on the studies of Magnus-Levi, Lewinski and Quick which demonstrated that a portion of benzoic acid, when ingested in large doses, is excreted as glyconic acid monobenzoate instead of quantitatively as hippuric acid and that the appearance of this reducing substance in the urine is a sign of glycine poverty of the

1. Cuthbertson, D. P., and Maclachlan, T. K.: The Treatment of Muscular Dystrophy with Glycine, Quart. J. Med. **3**: 411 (July) 1934.

2. Linneweh, W., and Linneweh, F.: Zur Frage des Glykokollmangels und der Glykokolltherapie bei progressiver Muskeldystrophie, Deutsches Arch. f. klin. Med. **176**: 526 (July 9) 1934.

organism. Two patients with unquestionable progressive muscular dystrophy and one normal person were investigated in this manner under controlled conditions of diet. The glycine supply and the glycine building power of the body were thus determined by the benzoic acid tolerance and it was established that no difference from the normal organism existed in this respect; therefore no true glycine deficiency exists. Consequently, glycine therapy is not a form of substitution therapy and its mode of action remains uncertain.

Careful chemical and clinical studies are gradually clarifying the underlying scientific and practical applications of an undoubted consistent chemical abnormality. Scientific medicine may again congratulate itself on the fruits of a well established mode of investigation.

"THROW-AWAY" MEDICAL PERIODICALS

The little magazines sent without subscription charge to various classes of readers are an interesting phenomenon. The complete costs of publication are of course borne by the advertisers. As might be expected, there is none too rigorous a control over the nature of goods advertised or the claims made in the advertising. Most of the advertising in such publications consists of the promotion of materials that could not possibly be accepted by the various councils and committees of the American Medical Association. A survey made of one of the most widely circulated free publications showed 85 per cent of the goods advertised as unacceptable to these rating bodies. From this point of view, then, these periodicals are a vicious menace to the high standards of medical practice in this country.

The "throw-away" called "Medical Economics" has appealed to the basest motives of those whom it attempts to reach, setting cash above conscience in medical practice. It seems much more concerned with the maintenance of income than with the maintenance of satisfactory standards of treatment. True, it devotes considerable space in its pages to the business aspects of medical practice. Regardless, however, of the extent to which other scientific periodicals may have been derelict in their failure to discuss such matters as collection of bills, the credit standings of patients, the outfitting of an office, or legal methods of enforcing payment, "Medical Economics" also attacks the ideals and principles of organized medicine and attempts to create disruption in medical thought. Its effect is an insidious attempt to undermine the councils and committees that have made therapy scientific and thereby rendered precarious the livelihood of promoters of nostrums.

A more recent comer in this field is a periodical called "Modern Medicine," emanating from Minneapolis. This purports to be a medical periodical along the lines of *Time* magazine. It falls somewhat short of the *Time* standard both in the method of presentation of material and in the quality of the material presented. Its advertising is for the most part of products that simply could not be accepted, yet it contains as an advisory board a list of leading names in the field of medicine, many of them officers of well established medical organizations. One wonders to what extent the services of these medical advisers are actually utilized. Are the names merely used in the promotion of the publication? There was a time when the names of vast numbers of doctors used to be put on periodicals to lend them status. Nowadays it is considered more reputable to refuse the use of one's name or to permit its use on an editorial board unless one is actually in some manner concerned with the policies of the periodical and the material it publishes.

A third class of periodical in the "throw-away" field is the one that purports to be a digest of medical literature, including either the abstracts or the condensations of medical articles. In the lay field such publications are sold by subscription and seem to serve a useful purpose.

For years manufacturers of proprietary medicine have been circulating house organs and other medical literature to physicians with the obvious intent of promoting interest in the drug field and particularly in the products which they manufactured. Such material was sent to the medical profession with the clear intent of selling goods. The new type of throw-away periodical has its intent concealed. It is thus not to be compared in its ethical status even with the type of house organ freely circulated by the proprietary medical interests. The mottoes of mankind for many centuries have warned against "something for nothing." "Beware the Greeks bearing gifts" goes back two thousand years.

THE EVALUATION OF SEROLOGIC PROCEDURES FOR THE DIAGNOSIS OF SYPHILIS

A plan, now under way, to evaluate independently in the United States serologic procedures for the diagnosis of syphilis has much to commend it. Briefly, it is proposed to collect and transport comparable specimens of blood from approximately 1,000 donors to all serologists of this country who have described an original modification of a complement fixation or a flocculation test. Specimens sent to serologists most distant from the point of collection will be forwarded by air mail, and delivery to nearby serologists will be purposely delayed so that the delivery time to all participants will coincide. Great care will also be exercised in the selection of the donors. The first group will consist of syphilitic patients who have received varying amounts of antisyphilitic treatment, and the third, or control group, of individuals who, on the basis of previous serologic and clinical examinations, are believed to be almost certainly not syphilitic. Consideration will also be given to the

influence of such diseases as tuberculosis, acute febrile diseases, leprosy, malignant growths and jaundice in the production of a positive serologic test. Specimens from such cases will be included in the third, or control, group if definite assurance can be obtained that the donor does not have syphilis.

An intelligent choice of patients in these several categories should serve as an accurate measure of specificity and sensitivity for all serologic tests for syphilis. Additional factors of importance in such an evaluation plan are the ease with which the procedures may be adopted by technicians generally, and their simplicity and rapidity of performance. No matter how effective a test may be in the hands of its originator, it cannot be regarded as reliable unless it can be applied with reasonable efficiency by other serologists and serologic technicians. Likewise, a test the technic of which is so simple and rapid that it can be performed daily is preferable to more complicated procedures of similar specificity and sensitivity.

The plan is fortunate in having the support of unprejudiced national organizations. It is sponsored by the United States Public Health Service, cooperating with the American Society of Clinical Pathologists. A committee consisting of five members—two clinical syphilologists of nation-wide reputation, two prominent members of the American Society of Clinical Pathologists, and an officer of the Public Health Service—will organize the project. The final reports from the participating serologists will also be interpreted by this committee on the basis of clinical information obtained from the individual donor.

Most American workers believe that the complement fixation test has been more highly developed in the United States than in any other part of the world. The efficiency of the American precipitation test was established by Kahn both at Copenhagen and at Montevideo. None of the American serologists who have described original modifications of the complement fixation test were represented at the other serologic conferences. The plan that is now proposed will permit a fair comparison of the best complement fixation and flocculation procedures in this country. It should not merely be of value in proving the efficacy of a given serologic procedure but should again focus the attention of the practicing physician on the importance of these tests in the diagnosis of syphilis. The information thus obtained should be made use of by the physician, the public health officer and others concerned with the important problem of the control of syphilis in assuring themselves that only the most specific and sensitive serologic procedures are employed.

The success of this plan is largely in the hands of the individual serologists. It is hoped that all such workers who have described an original modification of the complement fixation or the flocculation test will take part, and that such an evaluation plan may be held in the future at intervals of from three to five years. Only in this way will an accurate picture of the progress of the serology of syphilis be available to the medical profession.

Current Comment

THYROIDECTOMY IN DIABETES MELLITUS

The influence of the thyroid gland in diabetes has been recognized since Dumontpallier reported a case of glycosuria with exophthalmic goiter in 1867. As the goiter improved under treatment so did the diabetes. Since that time there have been isolated reports of various associations of the thyroid gland and diabetes. So far as is known, however, the recent report of Wilder, Foster and Pemberton [1] is the first of complete resection of the thyroid gland in an uncomplicated case of severe diabetes. The patient was a man, aged 26, who had had severe diabetes of eleven years' duration. His basal metabolism was normal (+ 5 and + 2 per cent). In spite of a rigidly restricted diet, about 45 units of insulin was required daily. Before the thyroidectomy he was placed on a diet of 2,300 calories, consisting of 103 Gm. of carbohydrate, 59 Gm. of protein and 183 Gm. of fat. An arbitrary dose of 10 units of insulin was given three times daily. The twenty-four hour excretion of dextrose in the urine on this regimen averaged 36 Gm. Following the operation, at which nearly all of the thyroid was removed, a small amount of thyroid tissue being left at the hilus of each lobe, progressive increase in sugar tolerance and progressive fall in basal metabolic rate were noted from about the tenth day. At dismissal, thirty days after the operation, the urine was practically sugar free with the patient on the previous diet with only 15 units of insulin daily. The basal metabolic rate was —29 per cent. Symptoms of myxedema appeared about sixty days after the operation. Twelve grains (0.8 Gm.) of desiccated thyroid was taken orally over a period of four days. The symptoms of myxedema disappeared promptly but the insulin requirement increased from 10 to 30 units. Two weeks after the desiccated thyroid was stopped the insulin requirement was back to 10 units, but thirty days later signs of myxedema recurred. This oscillation continued with the patient reporting dissatisfaction with the results six months later while taking from 8 to 10 units of insulin and one-tenth grain (0.006 Gm.) of desiccated thyroid daily. A year after the operation he wrote that he was comfortable, taking one-half grain (0.03 Gm.) of desiccated thyroid and from 14 to 16 units of insulin daily. This report serves as a good illustration of the substitution of one pathologic state for another. The interaction is self evident. With regard to the therapeutic procedure, few will be found to disagree with the patient and the authors that the improved sugar tolerance does not justify the production of a myxedematous state.

1. Wilder, R. M.; Foster, R. F., and Pemberton, J. de J.: Total Thyroidectomy in Diabetes Mellitus, Endocrinology **18**: 455 (July-Aug.) 1934.

Association News

ABSTRACT OF MINUTES OF MEETINGS OF BOARD OF TRUSTEES HELD IN CHICAGO, SEPTEMBER 20 AND 21

The Board of Trustees met in Chicago at the headquarters office on September 20, and at the Palmer House on September 21 during the Annual Conference of Secretaries of Constituent State Medical Associations.

COUNCIL ON PHYSICAL THERAPY

The Council on Physical Therapy, which had been invited to meet with the Board, attended the Thursday morning session and took part in a lengthy discussion of the work to be undertaken by that body.

USE OF PERIODIC HEALTH EXAMINATION FORM BY NATIONAL COMMITTEE ON GIRLS AND BOYS CLUB WORK

Permission was granted to the National Committee on Boys and Girls Club Work to use a modified form of the Association's periodic examination blank.

CHAIRMAN OF LOCAL COMMITTEE ON ARRANGEMENTS

The nomination of Dr. W. J. Carrington to act as chairman of the Local Committee on Arrangements for the Atlantic City Session of the Association was confirmed by the Board.

APPOINTMENTS

The following appointments were made: Dr. Frank Hammond Krusen to membership on the Council on Physical Therapy, with a view to complying with the resolution adopted by the House of Delegates at the Cleveland session of the Association providing for additional physical therapists on that body. Dr. Lydia Roberts to the Committee on Foods, to succeed Dr. James S. McLester, who is now President-Elect of the Association. Dr. H. Douglas Singer, editor-in-chief of the *Archives of Neurology and Psychiatry* to succeed Dr. T. H. Weisenburg (deceased). Dr. William H. Park, New York, and Dr. George M. Piersol, Philadelphia, to succeed themselves as representatives of the American Medical Association to the American Association for the Advancement of Science. Dr. Ludvig Hektoen and Dr. Urban Maes to succeed themselves on the Advisory Committee of the Committee on Scientific Exhibit. A committee composed of Drs. C. B. Wright, Rock Sleyster and Austin A. Hayden to confer with a similar committee of the American Dental Association on matters of mutual interest.

APPROPRIATIONS

Appropriations were made to enable the Committee on Mental Health to carry out its plans for the current year, and for subsidized and section exhibits in the Scientific Exhibit for the Atlantic City session.

EXPRESSION OF APPRECIATION TO NATIONAL BROADCASTING COMPANY

The appreciation of the Board was expressed for the courtesy of the National Broadcasting Company in granting the Association a fifteen minute period every Tuesday afternoon from 4 to 4:15 over its chain.

REQUEST FOR EXHIBIT FOR DEPARTMENT OF MEDICINE AND HEALTH OF MUSEUM OF SCIENCE AND INDUSTRY

A request from the Museum of Science and Industry for the Association's exhibit at A Century of Progress after the close of that exposition was granted, with the understanding that the exhibit will be placed in the Department of Medicine and Health.

PHYSICIANS SERVING ON ADVISORY BOARDS OF MEDICAL PERIODICALS

The acceptance on the part of physicians of membership on advisory boards of medical periodicals in the publication of which they have no voice was deprecated by the Board.

ENTERTAINMENT OF BRITISH PHYSICIANS IN 1935

Plans were arranged for the entertainment of members of the British Medical Association who come to the United States in August 1935 en route to the meeting of that Association in Australia.

MISCELLANEOUS BUSINESS

Various resolutions adopted by the House of Delegates were given consideration, and necessary steps were taken with a view to carrying out the provisions of those resolutions.

Numerous other matters were given attention and reports on many of these will be made later.

The Board adjourned, to meet in Chicago November 15 and 16.

MEDICAL BROADCASTS

Columbia Broadcasting System

The American Medical Association broadcasts on a western network of the Columbia Broadcasting System each Thursday afternoon on the Educational Forum from 4:30 to 4:45, central standard time. The next three broadcasts will be as follows:

October 25. What Is a Serum? W. W. Bauer, M.D.
November 1. The Common Drinking Cup, W. W. Bauer, M.D.
November 8. Your Child's Sleep, W. W. Bauer, M.D.

National Broadcasting Company

The American Medical Association broadcasts under the title "Your Health" on a Blue network of the National Broadcasting Company each Tuesday afternoon from 4 to 4:15, central standard time. The next three broadcasts will be as follows:

October 23. Reading About Health, W. W. Bauer, M.D.
October 30. Diphtheria Must Go, W. W. Bauer, M.D.
November 6. The Fight Against Appendicitis, W. W. Bauer, M.D.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

ARIZONA

Naturopathic Initiative Measure.—A naturopathic initiative measure will be voted on by the electorate of Arizona, November 6. This measure proposes to create a board of naturopathic examiners to examine and license naturopaths, to exempt naturopaths from the basic science requirement, to license without examination naturopaths who have been practicing in Arizona for three years, to license without examination naturopaths who hold "certificates" from the American Naturopathic Association, Arizona District, to authorize naturopaths to practice in any hospital supported by public funds, and to confer on naturopathic licentiates the right to practice the healing art without express limitations.

The Indian Service Physicians.—The Indian office, Washington, D. C., has approved the recent organization of the Indian Service Medical Society at Winslow with the following officers: Drs. Hudspeth E. Scoles, Tuba City, president; Marshall E. Burgess, Oraibi, vice president, and Le Roy Jones, Winslow, secretary. The area covered by the membership extends from the Consolidated Ute Agency with headquarters at Ignacio, Colo., through the Navajo country to Truxton Canyon Agency at Valentine, on the west. To date there are twenty members and six honorary members. The purposes of the society are to promote cooperation among service physicians and to enhance the value of their services to the government. All physicians and dentists of the U. S. Indian Service are eligible for membership. A meeting of the society was held at Fort Defiance, October 10.

CALIFORNIA

Another Veterans' Hospital Opened.—The new Veterans' Administration Facility in San Francisco has been opened. Dr. James G. Donnelly is manager of the institution, which has a capacity of 334 beds. A staff of ninety nurses and attendants has been assembled.

Infantile Paralysis Among Nurses.—The closing of the Orange County Hospital, Orange, October 4, to all except emergency cases was necessitated by an outbreak of infantile paralysis among the nurses. The normal nursing force numbers about forty. Five patients in the hospital have infantile paralysis, the Chicago *Tribune* reported.

Los Angeles County Given Health Award.—The American Public Health Association, at its recent annual meeting in Pasadena, presented to Dr. John L. Pomeroy, health officer of Los Angeles County, the Peter Ling Award. Each year the association presents the award to the county having the lowest infant mortality rate in the nation. For the fiscal year 1933-1934, there were thirty-eight infant deaths per thousand live births, newspapers reported.

Naturopath Placed on Probation.—Axel O. Lindstrom, a naturopath of San Francisco, was placed on probation for five years at a recent meeting of the California State Board of Medical Examiners, following a hearing of charges that he aided and abetted an unlicensed practitioner who operated the Gillberg Institute, 406 Sutter Street. At the same meeting of the board, the license of Will H. Coleman, naturopath, was revoked, on a charge of practicing beyond the limitation of his license.

Naturopathic Initiative.—A naturopathic initiative measure, to be voted on by the people of California, November 6, will, if adopted, create a public corporation to be known as the "Naturopathic Association of California." This corporation is to be vested with exclusive jurisdiction over naturopathy, conducting examinations and issuing licenses. Naturopathic licentiates will be given all the rights and privileges of any and all other practicing physicians of any class in the treatment of any and all diseases, injuries, deformities or other mental or physical conditions. The right to practice in all institutions supported wholly or in part by public funds will be accorded naturopaths.

DISTRICT OF COLUMBIA

University News.—Dr. Hans Lauber, professor of ophthalmology, University of Warsaw, Poland, addressed the faculty and students of George Washington University School of Medicine, October 2, on "Heredity, Particularly in Relation to the Eye."

Colonel Ashburn Appointed Hospital Superintendent.—Dr. Percy M. Ashburn, colonel, U. S. Army, retired, is now superintendent of Columbia Hospital for Women, Washington. Colonel Ashburn began his services with the army in 1898, and he was retired, Dec. 31, 1931. He is the author of "The Elements of Military Hygiene," 1909, and "History of the Medical Department of the United States Army," 1929.

GEORGIA

Appointments at University of Georgia.—New appointments to the full time faculty of the University of Georgia School of Medicine, Augusta, include the following:

Dr. Sam M. Brock, professor of surgery.
Dr. Evans B. Wood, assistant professor of gynecology and obstetrics.
William F. Hamilton, Ph.D., professor of physiology and pharmacology.
Everett S. Sanderson, Ph.D., professor of bacteriology and public health.
Fred A. Mettler, Ph.D., assistant professor of anatomy.
W. R. Brown, assistant professor of chemistry.
Robert A. Woodbury, Ph.D., assistant professor of physiology and pharmacology.
Robert B. Dienst, Ph.D., assistant professor of bacteriology and public health.

The new wing of the University Hospital, named for Milton Antony, who founded the school in 1828, was to have been completed about October 1. The building was made possible by a grant from the Public Works Administration and by funds contributed by the Alumni Association, the city of Augusta and the county of Richmond. It will have an outpatient department on the first floor and a contagious disease hospital on the second.

ILLINOIS

Society News.—At a special meeting of the Will-Grundy County Medical Society in Joliet, October 3, Drs. Joseph Colt Bloodgood, Baltimore, and Max Cutler, Chicago, were the speakers, on cancer. Dr. Philip Lewin, Chicago, addressed the society, October 10, on "Classification, Etiology and Treatment of Arthritis."——Dr. James H. Hutton, Chicago, addressed the DeWitt County Medical Society, October 4, on the endocrine aspects of essential hypertension.

Chicago

Dr. Leake to Lecture.—Dr. James P. Leake, senior surgeon, U. S. Public Health Service, Washington, D. C., will give an illustrated lecture before a joint meeting of the Institute of Medicine of Chicago and the Chicago Society of Internal Medicine at the Chicago Woman's Club, October 26. His subject will be "Poliomyelitis, with Special Reference to Epidemiology." Dr. Leake has been in California for several months studying the epidemic there.

Sir Harold Gillies Speaks at Northwestern.—The fourth annual Mayo Lecture in Surgery will be delivered by Sir Harold Gillies, London, at Thorne Hall, McKinlock Campus, Northwestern University School of Medicine, October 23. His subject will be "The Development and Scope of Plastic Surgery." Sir Harold is on the staffs of several hospitals, including St. Bartholomew's and St. Andrew's, London.

The Belfield Lecture.—Dr. Paul R. Cannon, professor of pathology, University of Chicago, will present the sixth annual William T. Belfield Lecture at the Palmer House, October 25, under the auspices of the Chicago Urological Society. His subject will be "Bacterial Localization." Preceding the lecture there will be a fellowship dinner at 6:30 p. m. in honor of Dr. Cannon, to which all members and guests of the society are invited. This lecture was established in 1929 in honor of Dr. Belfield, a founder of the Chicago Urological Society.

"The Common Cold."—The Chicago Medical Society will devote its meeting, October 24, to a symposium on the common cold, presented by the following physicians:

Russell L. Cecil, professor of clinical medicine, Cornell University Medical College, New York, Influenza and the Common Cold.
Frank Jirka, director, state department of health, Springfield, Field Studies of the Common Cold.
William W. Bauer, director, bureau of health and public instruction, American Medical Association, The Economic Cost of the Common Cold.
Walter H. Nadler, associate professor of medicine, Northwestern University School of Medicine, Treatment, Complications and Sequelae of the Common Cold.

The evening has been designated "General Practitioner's Night." Dr. Edward H. Ochsner will give a demonstration prior to the symposium on x-ray carcinoma of the hands.

Dr. Jordan Awarded Medal.—Edwin O. Jordan, Ph.D., formerly chairman of the department of hygiene and bacteriology, University of Chicago, was awarded the Sedgwick Memorial Medal for distinguished service in public health at the annual meeting of the American Public Health Association in Pasadena in September. Although he retired officially from the university in 1933, after forty-one years' service, Dr. Jordan has been offering graduate courses and has continued his research in the department of hygiene and bacteriology. He had been chairman of the department since it was set up in 1914, and professor since 1907. He is editor of the *Journal of Preventive Medicine* and joint editor of the *Journal of Infectious Diseases*. He is a former president of the Society of American Bacteriologists and the American Epidemiological Society. He is the author of many volumes on bacteriology and related subjects, and co-author of a biography of W. T. Sedgwick, for whom the medal is named.

INDIANA

Many Years in Practice.—A recent meeting of the Grant County Medical Society was devoted to honoring the following physicians who had been in practice forty years or longer: John C. Knight, Jonesboro; Leander H. Conley, Gas City; John F. Loomis, Marion; William A. Fankboner, Marion; William S. Resoner, Swayzee; Nettie B. Powell, Marion; Edwin M. Trook, Marion, and Zed T. Hawkins, Fairmount.

Meeting of Anesthetists.—Twenty-eight physician-anesthetists, from all sections of the state, assembled for a dinner meeting at Purdue University, Lafayette, September 11, to establish contact between Purdue Research Foundation and the practicing specialists in anesthesia. Speakers included Dr. Franklin S. Crockett, Lafayette, who discussed the recent ruling of the state board of medical examiners that the administration of an anesthetic was in fact medical practice. A petition was signed, looking toward the organization of a section in anesthesia in the state association, according to the *Journal of the Indiana State Medical Association*.

Society News.—A symposium on rheumatic fever will be presented before the Indianapolis Medical Society, October 23, by Drs. Russell R. Hippensteel, George S. Bond and Horace M. Banks. Dr. Roy W. Scott, Cleveland, will address the society, October 30, on "Modern Aspects of the Problem of Vascular Disease." A symposium on foreign bodies in the lungs constituted the program of the society, October 2; Drs. Lyman T. Meiks, Cecil S. Wright and Delbert O. Kearby were the speakers.——Dr. Otis C. Higgins, Lebanon, discussed encephalitis before the Boone County Medical Society at Lebanon, October 2.——At a meeting of the Hendricks County Medical Society in Danville, September 28, Frederic R. Henshaw, D.D.S., dean, Indiana University School of Dentistry, spoke on the relation of medicine to dentistry.——The Porter County Medical Society was addressed at Valparaiso, September 25, by Dr. Sidney A. Portis, Chicago, on "The Medical Management of Gallbladder Disease."——The Delaware-Blackford County Medical Society was addressed in Muncie, September 18, by Dr. Henry E. Bibler, Muncie, on encephalitis.

IOWA

Society News.—Speakers before the Jackson County Medical Society, August 2, were Drs. Dean M. Lierle and Nathaniel G. Alcock, Iowa City, on "Otolaryngology from the Standpoint of the Practitioner" and "Resection Method in the Treatment of Diseases of the Prostate," respectively.—— Dr. Russell L. Cecil, New York, will speak before the Linn County Medical Society, October 25, on arthritis. Dr. Joseph B. DeLee, Chicago, addressed the society in Cedar Rapids, October 4, and showed motion pictures on forceps operations and episiotomy; Dr. James Stuart McQuiston, Cedar Rapids, presented a paper on "Functional Diseases and General Medicine."

KANSAS

Society News.—Dr. Clifford C. Nesselrode, Kansas City, addressed the Southeastern Kansas Medical Society in Chanute, September 13, on cancer.—— Dr. Kerwin Armand Fischer, Arkansas City, addressed the Cowley County Medical Society in Winfield, September 20, on "Injuries to the Navicular Bone," and Dr. Fred E. Torrance, Winfield, syphilis.—— Dr. Edward T. Gibson, Kansas City, Mo., addressed the Lyon County Medical Society at Emporia, September 4, on "Treatment of Head Injuries."

State Cancer Program.—Plans for an educational program against cancer were recently adopted by the Kansas Federation of Women's Clubs at a meeting addressed by Dr. Earle G. Brown, secretary of the state board of health and state chairman of the American Society for the Control of Cancer. Other speakers were J. Scott Walker, D.D.S., Chetopa, president of the state dental society, and Dr. Clifford C. Nesselrode, Kansas City, chairman of the cancer committee of the state medical society. According to the *Bulletin* of the American Society for the Control of Cancer, a three year health program emphasizing cancer control is anticipated.

KENTUCKY

Personal.—Dr. Jacob Leland Tanner, Albany, has been appointed health officer of Henderson County.——Dr. Herman T. Carter, Gilbertsville, has been chosen health officer of a new health unit to be established in Metcalfe County.—— Dr. John G. South, Frankfort, has been named chief of the bureau of registration of the state board of health, it is reported.

Society News.—Dr. Derrick T. Vail Jr., Cincinnati, addressed the Louisville Eye and Ear Society, October 11, on "The Ophthalmologist Looks at Dacryocystorhinostomy."—— Dr. Oscar O. Miller addressed the Louisville Medico-Chirurgical Society, October 12, on silicosis. Dr. James Royden Peabody will speak, October 26, on "Diagnosis and Treatment of Brain Abscess of Otitic Origin."——Dr. Stephen C. McCoy will be the speaker at a meeting of the Louisville Urological Society, October 30, on "Renal Resection."—— Dr. William Barnett Owen addressed the Society of Physicians and Surgeons of Louisville, October 18, on osteomyelitis.

LOUISIANA

Personal.—Dr. Glenn J. Smith recently resigned as superintendent of the East Louisiana State Hospital at Jackson, a position he had held since 1929; he has been succeeded by Dr. John A. Thames, Natalbany.——Dr. Walter W. Poimboeuf, Bastrop, has been appointed director of the St. Landry Parish Health Department, with headquarters at Opelousas.

Resolution Urges Health Unit Be Discontinued.—In a resolution adopted at a special session in Opelousas, August 29, the St. Landry Parish Medical Society declared itself opposed to the continued operation of the local health unit and asked that the old system of the appointment of a health officer be adopted. The resolution states that there have been numerous complaints against the encroachment of the health unit on the legitimate interests of the practicing physicians of the parish, and suggests that the appropriation to maintain the unit be discontinued.

Society News.—Dr. Rudolph H. Kampmeier, New Orleans, addressed the Second District Medical Society at Norco, September 16, on diagnosis and treatment of infections of the respiratory tract.——At a meeting of the Concordia-Catahoula Bi-Parish Medical Society in Jonesville, September 6, Dr. Naum G. Nasif, Jonesville, discussed diathermy in the treatment of lobar pneumonia.——The Orleans Parish Medical Society was addressed in New Orleans, October 8, by Henry T. Scott, Ph.D., Madison, director, biologic research, Wisconsin Alumni Research Foundation, on "Light and Its Application to the Irradiation of Foods."

MARYLAND

Personal.—Dr. Francis Dana Coman, Baltimore, sailed, August 22, for Honolulu en route to New Zealand to join the Antarctic expedition of Lincoln Ellsworth. Dr. Coman accompanied Rear Admiral Richard E. Byrd on his first expedition to the Antarctic.

Semiannual Meeting.—The Medical and Chirurgical Faculty of Maryland held its semiannual meeting at Point Lookout, October 11-12. Dr. Leonard B. Johnson, Morganza, president, St. Mary's County Medical Society, gave the address of welcome, and Dr. George O. Sharrett, Cumberland, president of the medical faculty, the response. The scientific session was given over to papers by Drs. Eugene L. Flippin on "Roentgen Findings in Primary Malignancy of the Lung"; Howard E. Ashbury, "Management of the Cancer Patient," and Sydney R. Miller, "Present Concepts of the Diagnosis and Therapy of Chronic Nephritis."

Society News.—The Baltimore City Medical Society was addressed, October 19, by Drs. Adolph Weinzirl on "The Diphtheria Prevention Campaign in Baltimore"; John T. King Jr., "Factors in the Etiology of Hypertension," and Harvey B. Stone and James C. Owings, "Living Grafts and Thyroid and Parathyroid Glands."——Dr. Newton W. Hershner, Mechanicsburg, Pa., was elected president of the Cumberland Valley Medical Association at its thirty-second annual meeting in Hagerstown in September. Other officers elected are Drs. Henry C. Lawton, Camp Hill, Pa., and Julius E. Kempter, Chambersburg, Pa., vice presidents, and Drs. William A. Gordon, Hagerstown, and Percy D. Hoover, Waynesboro, Pa., secretary and treasurer, respectively.

MASSACHUSETTS

Committee on Research in Dental Medicine.—A committee on research in dental medicine comprising seven representatives of the faculty of arts and sciences and the medical and dental schools has been appointed at Harvard University. The committee has been given general supervision over research in the dental school. Its purposes will be to promote important dental research, act as a clearing house for research that is important to other fields, and to provide official contacts through which the dental school can readily get assistance for its research problems that overlap those of other departments. A grant from the Milton Fund has been given to the committee for work on its first problem, which will deal with the effects of nutrition on teeth and their supporting structures. Members of the new committee are Elmer P. Kohler, Ph.D., Abbott and James Lawrence professor of chemistry; Alfred C. Redfield, Ph.D., professor of physiology and director of the Biological Laboratories; Dr. Simeon B. Wolbach, Shattuck professor of pathologic anatomy, and consulting pathologist to the Cancer Commission of Harvard University; Dr. Walter B. Cannon, George Higginson professor of physiology; Percy R. Howe, S.D., Thomas Alexander Forsyth professor of dental science, and instructor in pathology, Harvard Medical School; Lawrence W. Baker, D.M.D., professor of orthodontia, and George P. Matthews, D.M.D., instructor in anatomy. Dr. Leroy M. S. Miner, dean of the dental school, will serve as a member ex officio of the committee.

MINNESOTA

Trudeau Celebration.—Dr. James Burns Amberson Jr., New York, was the guest speaker in the celebration of the Minnesota Trudeau Medical Society, October 6, to observe the eighty-sixth anniversary of the birth of Dr. Edward Livingston Trudeau. Dr. Trudeau was born, Oct. 5, 1848. Dr. Amberson's subject was "Estimation of the Healing Process in Pulmonary Tuberculosis and Its Importance in Treatment." The tribute to Dr. Trudeau was made by Dr. Walter J. Marcley, Minneapolis.

MISSISSIPPI

Society News.—At a meeting of the Issaquena-Sharkey-Warren Counties Medical Society in Vicksburg, September 11, speakers included Dr. George W. Gaines, Tallulah, La., on "Streptococcic Sore Throat."—— Dr. Edgar Burns, New Orleans, addressed the Pike County Medical Society, recently, on genito-urinary tuberculosis.—— Speakers before the Tri-County Medical Society at Monticello, September 11, were Drs. John W. Wilson, Monticello, on significance of adenitis; John R. Markette, Brookhaven, what vomiting may indicate, and Oscar N. Arrington, Brookhaven, hematuria. The next meeting of the society will be held in Brookhaven, December 10. ——A clinical pathologic conference on heart disease was a feature of the meeting of the Northeast Mississippi Thirteen

Counties Medical Society at Houlka, September 12; guest speakers were Drs. James S. McLester, President-Elect of the American Medical Association, and George S. Graham, Birmingham, Ala. Other speakers on the program were Drs. Theodore H. Rayburn, Pontotoc, on subphrenic abscess; William T. Pride, Memphis, Tenn., conduct of a normal labor case, and Douglas D. Baugh, Houston, recognition of common mental disorders.

Illegal Practitioners Investigated.—The Mississippi State Board of Health has provided the following news about certain illegal practitioners: Affidavits were made against "Dr. C. Hester," McCall Creek, July 9, for practicing medicine without a license. Investigation disclosed that he had obtained a copy of the license of Dr. Charles F. Hester from the records in the circuit clerk's office at Philadelphia and passed himself off as this physician. He filed this copy of the license with the circuit clerk at Meadville. It is reported that he pleaded guilty, paid his fine and court costs and was to have left the state; however, it was stated that he is still practicing. He had been arrested and charged with obtaining a narcotic license fraudulently. Dr. Charles F. Hester, now living in Amarillo, Texas, is the only physician with this name ever licensed to practice in Mississippi. He testified at the trial of the impostor. "Dr." R. C. Watts, colored, was tried, July 10, at Anguilla, on a charge of practicing medicine without a license; he was convicted, the fine being suspended on condition that he would leave and stay out of the state. Richard Tigue, colored, was tried before a justice of the peace near Louisville, August 18, for practicing medicine without a license. He was charged with delivering a woman in labor. The attorney who pleaded his case endeavored to show that no fee was paid for the service. Tigue was convicted and fined $200; the verdict was appealed to the circuit court of Winston County. Joe Hatton, colored, has been acting as a midwife for colored women in Jones County for several years. He pleaded guilty in his trial before a justice of the peace at Soso and was given a suspended fine of $200 on condition that he refrain from this practice. Other investigations are being conducted in Coahoma, Hinds, Lafayette, Pearl River, Rankin, Tippah and Winston counties. The state board of health urges practicing physicians to cooperate with it in this campaign against illegal practitioners.

NEW JERSEY

Society News.—Drs. George T. Pack, New York, and Samuel M. Beale, Sandwich, Mass., addressed the Bergen County Medical Society, Hackensack, September 11, on "Recent Advances in Cancer Research" and "Small Doses of Insulin," respectively. Dr. Edward J. Donovan, New York, addressed the society, October 9, on "Abdominal Surgery in Children."——Dr. William D. Haggard, Nashville, Tenn., addressed the Atlantic County Medical Society, Atlantic City, October 12, on "The Delayed Operation for Appendicitis in Delayed Cases—An Analysis of 3,225 Operative Cases."——Dr. S. Bernard Wortis, New York, addressed the Hudson County Medical Society, Jersey City, October 2, on "Head Injuries—Treatment and Evaluation."

NEW YORK

Personal.—Dr. Henry R. O'Brien, Oberlin, Ohio, recently health commissioner of Lorain County, Ohio, has been appointed assistant district health officer on the staff of the New York State Department of Health.——Dr. William A. Howe, chief of the medical inspection bureau of the state education department, retired October 1, after being associated with the department since 1915.——Dr. Philip J. Rafle of the staff of the state department of health, has been appointed temporary district health officer with headquarters in Syracuse until a successor to the late Dr. Frederick W. Sears is selected by civil service examination.——Colleagues of Dr. Edward R. Baldwin, director of the Edward L. Trudeau Foundation, Saranac Lake, marked his seventieth birthday, September 8, by presenting him an armchair. Dr. James Woods Price made the presentation speech at a gathering at Dr. Baldwin's home in the evening, attended by about twenty-five physicians and others.

New York City

Society News.—Among speakers at a meeting of the Society for Experimental Biology and Medicine, October 17, were Drs. Irving Sherwood Wright, on "Treatment of Adult Scurvy with Crystalline Vitamin C (Ascorbic Acid)"; Alfred N. Richards, Ph.D., Benton B. Westfall, Ph.D., and Phyllis A. Bott, Philadelphia, on "Renal Excretion of Insulin, Creatinine and Xylose in Normal Dogs."——Dr. Mortimer N. Hyams gave an afternoon lecture before the Medical Society of the County of Queens, October 5, on "Sterilization of the Female by Coagulation."——Dr. John L. Rice, health commissioner of New York, addressed a joint meeting of the Medical Society of the County of Queens and the Queensboro Tuberculosis and Health Association at Forest Hills, September 26, on "Municipal Control of Tuberculosis."

Hospital Planning Board Established.—Planning of hospital buildings under the jurisdiction of the city department of hospitals will henceforth be under the control of a board of planning and construction set up by Dr. Sigismund S. Goldwater, hospital commissioner, October 11. Responsibility for critical examination of building plans will be vested in a board made up of the following: the medical superintendent of the department, a representative of the division of engineering, the head of the division of nursing and the head of the division of dietetics. In addition, the department's director of laboratories and director of roentgenology will be associate members, and the superintendent of the individual hospital affected in any case will be a member ex officio. In the future plans for hospitals will not be accepted until they have received the written approval of this board, it was said.

OHIO

State Medical Election.—Dr. Ralph R. Hendershott, Tiffin, was chosen president-elect of the Ohio State Medical Association at the annual session in Columbus, October 4-6. Dr. John A. Caldwell Jr., Cincinnati, became president. The 1935 meeting will be held in Cincinnati.

Anniversary of Library Association.—The fortieth anniversary of the founding of the Cleveland Library Association was celebrated at a dinner in honor of its charter members at the Allen Memorial Library Building, October 19. Dr. William E. Bruner gave a talk on the founding of the library and Dr. Howard T. Karsner, an appreciation of surviving charter members.

Third Graduate Course.—The Cleveland Academy of Medicine will present its third graduate course beginning October 26 and continuing weekly until March 22. The course this year is in the general field of obstetrics and gynecology. The first eight lectures will be as follows:

October 26, Physiology of the Female Genital Organs Including Endocrinology, Dr. Robert L. Faulkner.
November 2, Functional Disorders of Menstruation, Dr. Gerald B. Hurd.
November 9, Sterility, Dr. James L. Reycraft.
November 16, Diseases of the Ovary, Dr. Marion D. Douglass Jr.
November 23, Diseases of the Uterus, Dr. William D. Fullerton.
December 7, Carcinoma of the Cervix and Radium Treatment, Dr. Lawrence A. Pomeroy.
December 14 and 21, Nonoperative Treatment of Gynecologic Conditions, Dr. William H. Weir.

OREGON

Cult Initiative Measure.—On November 6, the electorate of Oregon will vote on a proposed initiative measure to adopt a "healing arts amendment" to the constitution of the state. This constitutional amendment, if adopted, will abolish the requirements that all practitioners of the healing art shall demonstrate their fitness in anatomy, physiology, pathology, chemistry and hygiene before a nonsectarian, impartial board. It will confer on examining boards and schools of drugless healers the right to enlarge the scope of practice of drugless healers at will. It will permit injured employees to select any physician, including drugless healers, to treat their injuries. It will require all hospitals to admit any practitioner of the healing art, including drugless healers, selected by any injured or sick person to the hospital. It will deprive the legislature of Oregon of any further jurisdiction over the practice of the healing art in the state.

PENNSYLVANIA

Society News.—Dr. George W. Ramsey, Washington, addressed the Washington County Medical Society, October 10, on acute pancreatitis.——Dr. Harry Ryerson Decker, Pittsburgh, addressed the Fayette County Medical Society, Uniontown, October 11, on treatment of pulmonary infection.——Dr. John P. Henry, Pittsburgh, gave a clinical demonstration of the injection treatment of varicose veins before the Cambria County Medical Society, Johnstown, October 11, and Dr. Bernard J. McCloskey, Johnstown, discussed "Treatment of Empyema by Aspiration."——Dr. Horace B. Anderson, Johnstown, addressed the Bedford County Medical Society, September 20, on heart failure.——Dr. Harold A. Miller, state director of emergency medical relief, Harrisburg, addressed the Delaware County Medical Society, October 11, on "The Present Social Order in Its Relation to Medical Care Given to the Indigent and the Necessity for Study of Alternate Methods with the Thought of Constructing a Program Agreeable to All."

Philadelphia

Society News. — Dr. Maurice N. Richter, New York, addressed the Pathological Society of Philadelphia, October 11, on "Experimental Aspects of Leukemia."——Speakers at a meeting of the Philadelphia Roentgen Ray Society, October 11, were Drs. Barton R. Young and William Edward Chamberlain, on "Hodgkin's Disease: A Clinical and Roentgenologic Review," and Wendell C. Hall, "Roentgenologic Significance of 'Milk of Calcium' Bile."——Dr. Alfred Gordon, among others, addressed the Philadelphia Psychiatric Society, October 12, on "Epilepsy and Arteriosclerosis."

Discussion of Hospital Problems.—The regular meeting of the Philadelphia County Medical Society, October 10, was devoted to discussion of hospital problems. E. H. Lewinski-Corwin, Ph.D., New York, discussed "The New York Hospital Situation"; Mr. Charles F. Neergaard, hospital consultant, New York, "The Hospital Situation with Special Reference to Philadelphia"; Dr. Harold A. Miller, state director of emergency medical relief, "Alternative Methods of Medical Functioning in Relation to the Indigent," and Mr. Louis I. Matthews, superintendent of St. Luke's and Children's Hospital, "Lay and Professional Relationships in Hospitals."

TENNESSEE

Flexner Lectures at Vanderbilt. — Prof. Erik Gunnar Nyström, professor of surgery at the University of Upsala, Sweden, will give the fourth series of the Abraham Flexner Lectures at Vanderbilt University School of Medicine, Nashville, in February and March, 1935.

Society News. — Dr. James R. Reinberger, Memphis, addressed the Hamilton County Medical Society, Chattanooga, September 27, on "Results in Repair of Relaxed Perineum at Time of Delivery."——Drs. Horace B. Cupp and Carroll H. Long, Johnson City, addressed the Washington County Medical Society, October 4, on "Backache: A Problem in Ex-Service Men" and "Diagnosis and Treatment of Endocrine Disorders in the Female," respectively.——Dr. C. C. Hacker was recently elected mayor of Elizabethton.——Dr. Hugh J. Morgan addressed the Nashville Academy of Medicine, October 2, on "Factors Conditioning the Transmission of Syphilis by Blood Transfusion."

District Meeting.—The third district of the Tennessee State Medical Association held a meeting in Chattanooga, September 28, with Dr. James S. McLester, Birmingham, Ala., President-Elect of the American Medical Association, as the guest of honor. Dr. McLester delivered an address on "Recent Advances in Our Knowledge of the Deficiency Diseases" at the scientific meeting and spoke at an evening banquet. Other speakers included Drs. Gilbert Madison Roberts, Chattanooga, on "Transurethral Prostatic Resection"; Robert P. Ball and Stanton S. Marchbanks, Chattanooga, "Roentgen Examination in Obstetrics" and William E. Van Order, Chattanooga, "Abdominal Pain in Children."

WASHINGTON

State Medical Election. — Dr. Nathan L. Thompson, Everett, was elected president of the Washington State Medical Association at the annual session in Corvallis, September 12. Dr. Curtis H. Thomson, Seattle, was reelected secretary. The 1935 meeting will be held in Everett.

GENERAL

International Radiologic Congress. — Dr. Arthur C. Christie, Washington, was elected president of the International Congress of Radiology at the recent session in Zurich, Switzerland, and it was decided to hold the next congress in the United States in 1937, possibly in Chicago. Dr. Benjamin H. Orndoff, Chicago, was elected general secretary.

Saunders Memorial Medal.—Recommendations for candidates for the 1935 Walter Burns Saunders Memorial Medal should be sent to the headquarters of the American Nurses' Association, 50 West Fiftieth Street, New York, before December 31. This medal is given for distinguished service in the cause of nursing. Rules governing eligibility may be obtained from the association.

Society News. — The annual conference of the National Society for the Prevention of Blindness will be held in New York, December 6-8. Subjects selected for discussion will be causes of blindness, sight saving classes, prevention of eye accidents, and prevention of prenatal accidents that may cause blindness. Dr. Edward Jackson, Denver, will make the principal address, on "A Wide Basis for Blindness Prevention."——Dr. John Shelton Horsley, Richmond, Va., was elected president of the American Society for the Study of Neoplastic Diseases at its meeting in Washington, September 6-8, succeeding Dr. Max Cutler, Chicago. Dr. Charles F. Geschickter, Baltimore, was named vice president and Dr. Eugene R. Whitmore, Washington, D. C., secretary.

Death Rates in Large Cities.—An analysis of the vital statistics of twenty-eight large cities made by the New York City Department of Health shows a general death rate for 1933 of 10.95 per thousand of population. Washington, D. C., had the highest rate (15.89) and Milwaukee, the lowest (8.23). Among the five largest cities Chicago had the lowest infant mortality rate (49); the lowest rates in the group were for Seattle, Portland, Ore., and Oakland, Calif., each 38 per thousand live births. The highest rates were for Buffalo, N. Y., and Columbus, Ohio, each 69. The highest rates for some important causes of death were as follows: cancer, Boston, 176 per hundred thousand; pulmonary tuberculosis, Washington, D. C., 103.2; diabetes, Jersey City, N. J., 36.6; typhoid, Washington, 3.6; diphtheria, Louisville, Ky., 10.4; suicides, San Francisco, 37.6; homicides, Houston, Texas, 26.1; automobile accidents, Los Angeles, 36.2. Lowest rates for the same causes were: cancer, Houston, 70.3; pulmonary tuberculosis, Minneapolis, 14.7; diabetes, Houston, 10.3; typhoid, Portland, Ore., none; diphtheria, Seattle and Rochester, N. Y., none; suicide, Jersey City, 8.3; homicide, Milwaukee, 2.2; automobile accidents, Rochester, N. Y., 13.8.

World Prevalence of Smallpox.—Figures assembled by the Health Section of the League of Nations showing the distribution of smallpox throughout the world during the past two years indicate a noticeable decline in the United States. The total number of cases reported in 1933 was 6,233, as against 49,000, 30,000 and 11,000 during the previous three years. A study of the regional distribution shows that the disease is rare in the Northeastern states, relatively high in the Central and Southern states and highest in the Far West. Elsewhere in North America smallpox is also on the decline but still causes several thousand deaths each year in Mexico. Portugal and the Soviet Union are the only important smallpox foci in Europe; in both countries it appears to be of the serious type, according to the report, whereas in many countries the mortality is extremely low. In 1933 Egypt had the most serious epidemic of smallpox in Africa, with 5,697 cases and nearly 1,000 deaths; it has definitely declined during 1934. The number of cases rose in the Belgian Congo from 1,241 in 1931 to 3,410 in 1933. In Asia the most important focus is British India, for which provisional figures showed 250,000 cases in 1933. In the ports of China, where there was an epidemic in the winter of 1932-1933, the disease remained endemic, with a slight rise in Shanghai in the early months of this year. Japan has also had an increase after being comparatively free for several years.

CANADA

Personal. — Dr. James A. Faulkner, Belleville, has been appointed minister of health for Ontario, succeeding Dr. John M. Robb. Dr. John M. Uhrich, Regina, has been appointed minister of public health for Saskatchewan.——Dr. Alberic Marin was recently elected president and Dr. Paul H. Poirier, secretary, of the Montreal Dermatological Society.

Society News. — At the annual meeting of the British Columbia Medical Association in Kamloops, September 17-18, the speakers included: Drs. James C. Masson, Rochester, Minn., on "Malignancy of the Large Bowel" and "Use of Living Sutures in the More Difficult Abdominal Herniae"; William P. Murphy, Boston, "Therapeutic Effects of Intramuscular Injections of Liver Extract," and Francis M. Pottenger, Monrovia, Calif., "Rôle of the General Practitioner in Diagnosis of Tuberculosis."

Bar Sale of Dinitrophenol.—Changes in the Food and Drugs Act to correct discrepancies between it and the Proprietary or Patent Medicine Act were enacted by the recent federal parliament and will go into effect Jan. 1, 1935, according to the *Canadian Medical Association Journal*. The principal change was to insert in the Food and Drugs Act a list of nearly forty diseases for which remedies cannot be sold. The journal points out that since obesity is one of the conditions listed, the sale of dinitrophenol would appear to be barred.

CORRECTION

A Defense of Suprapubic Prostatectomy.—In a letter on prostatectomy by Dr. E. L. Keyes (THE JOURNAL, October 6, p. 1086, column 1, bottom of page), the statement "172 suprapubic cystotomies" should be "172 suprapubic prostatectomies."

Foreign Letters

LONDON

(From Our Regular Correspondent)

Sept. 22, 1934.

The International Sanitary Control of Aerial Navigation

The government has published the report of the International Sanitary Convention for Aerial Navigation, which has been signed by most of the important countries of the world. If the regulations adopted are properly carried out, the risk of conveyance of disease from one country to another should be minimized. Each country undertakes to provide at its aerodromes a sanitary organization adapted to the current needs of prophylaxis, which as a minimum will consist of the attendance of a physician at such times as may be necessary for the medical examinations contemplated by the convention. It rests with each country to take into account the risk of infectious disease to which its territory may be exposed and to decide whether to establish sanitary aerodromes, which will have an organized medical service with one medical officer and one or more sanitary inspectors, who will not necessarily be in constant attendance. The sanitary aerodrome will have (1) equipment for taking and dispatching suspected material for examination in a laboratory, if such examination cannot be made on the spot; (2) facilities for the isolation and care of the sick, for the isolation of contacts separately from the sick, and for the carrying out of disinfection and deratization. In the journey log of the aircraft the following must be entered: 1. Any facts relevant to public health which have arisen in the course of the voyage. 2. Any sanitary measures undergone by the aircraft before departure or at places of call, in application of the present convention. 3. Information concerning the appearance in the country of departure of the following infectious diseases: plague, cholera, yellow fever, typhus and smallpox. If any of these diseases appear in a noninfected country, the aerodrome authorities shall enter the information in the journey log of any craft leaving it during a period of fifteen days from the receipt of the information. The medical officer of the aerodrome has the right of sanitary inspection of the passengers and crew, and on his advice the embarkation of persons with symptoms of infectious diseases may be prohibited. Aircrafts in flight are forbidden to let fall matter capable of causing an outbreak of infectious disease.

REGULATIONS APPLICABLE TO CERTAIN INFECTIOUS DISEASES

Plague, cholera, yellow fever, typhus and smallpox are subject to special measures. For purposes of the convention the period of incubation of plague is reckoned as six days, of cholera five days, of yellow fever six days, of typhus twelve days, and of smallpox fourteen days. The measures to be adopted on the departure of an aircraft from a local area infected by plague, cholera, typhus or smallpox are (1) thorough cleansing of the aircraft, (2) medical inspection of passengers and crew, (3) exclusion of any person showing symptoms of these diseases as well as of persons in such close relation with the sick as to be liable to transmit these diseases, (4) inspection of personal effects, which shall be accepted only if in a reasonable state of cleanliness, (5) in case of plague deratization, if there is any reason to suspect the presence of rats on board. On arrival from such infected areas the aircraft may be required to land at a prescribed sanitary or authorized aerodrome and the movements of the passengers and crew may be restricted. If there is on board a recognized or suspected case of plague the following measures are applicable: (1) immediate disembarkation of the sick, (2) surveillance of contacts and suspects for a period not exceeding six days, (3) disinfection and disinsectization of personal effects, and (4) deratization. For a case of cholera the measures are similar except that the period of surveillance is five days and the drinking water may be disinfected and emptied. For typhus the measures are similar except for delousing and surveillance for twelve days after this. For smallpox the special measures are vaccination and surveillance for a period not exceeding fourteen days of those on board. In regions in which yellow fever has occurred or is endemic aerodromes must be at an adequate distance from the nearest inhabited center, provided with a water supply protected against mosquitoes and with mosquito-proof dwellings for the aircraft crews and for the accommodation of passengers. The aircraft and cargo must be inspected to see that they do not contain mosquitoes and, if necessary, disinsectized. Passengers and crew may be put under surveillance for six days from exposure to infection.

New Regulations for the Dusty Industries

New and more stringent regulations have been made by the government for the dusty industries, which include the refractories, sandstone, pottery and asbestos. Those seeking employment in these industries must be examined by a member of the medical board. Their employment will not be allowed if their physique does not satisfy the following requirements: 1. The chest must be at least of average development and the respiratory passages free from obstruction. 2. There must be no sign of disease of the lungs or heart. 3. There must be no tuberculosis in any region.

PARIS

(From Our Regular Correspondent)

Sept. 12, 1934.

A New Vaccine Against Plague

Important research on vaccination against plague has been carried out in Madagascar, in the Institut Pasteur de Tananarive, by Girard and Robic, the results of which were recently reported by Professor Mesnil to the Academy of Medicine. The vaccines against plague at present in use are prepared from cultures of killed bacilli, which confer an immunity of only a few weeks duration. The soldiers who are vaccinated before they leave the capital lose the greater part of their immunity by the time they reach their destination in the colonies and it is often necessary to repeat the vaccinations, which sometimes give rise to unpleasant anaphylactic reactions. Girard and Robic have prepared a new vaccine, with living bacilli derived from strains that have been attenuated by many successive cultures, according to the method that Calmette employed in the preparation of the B C G vaccine against tuberculosis. With this new vaccine they have vaccinated 15,000 persons among the population of the high plateaus of Madagascar, where both the pulmonary and the bubonic form of plague is rather frequent, with a high mortality. From March 1 to April 15, an average of 150 new cases per week was recorded, only a third of which were of the bubonic type. No untoward incidents were observed following the vaccinations. No vaccinated persons have contracted the plague as yet, although many were living in infected surroundings. It would seem that, owing to these measures, the epidemic will be eradicated soon.

Tuberculosis in the Army

The detection of tuberculosis among the young men who are enlisted by conscription for the army is a matter of great importance. The law has decided that any soldier who is declared by the army physicians to be in perfect health on his arrival at the barracks, and who later becomes tuberculous, is assumed to have contracted the disease during his military service, which fact not only entitles him to an immediate discharge from the army but also to a pension for the remainder of his life. This constitutes a heavy burden on the budget.

Hence the army physicians are urged to exercise great care in the examination of recruits, each of whom must undergo two examinations. The first examination is given at the time the young conscript presents himself for the first time to the registration officers the day before his enlistment. This examination is a hasty and summary proceeding, being public and extending over only a few minutes. It enables the examiners to eliminate only those who are inacceptable at first sight, by reason of undersize, insufficient chest development, deformities, albuminuria, diabetes and the like. Following this examination, conscripts are accepted only provisionally and assigned to their respective units. Thereupon the chief physician of the regiment proceeds with an individual detailed examination. He is allowed a period of three months in which to complete his examinations, and he may, if he deems it necessary, send any recruit for a consultation with specialists in the military hospitals of the nearest large city. It often requires shrewdness to detect the simulators. Formerly it was common for some to simulate deafness, excessive myopia or dysentery in order to be relieved of military service. Since the enactment of the new law the reverse is true. Now the simulators seek to conceal any disease with which they are affected in order not to reveal it until after two examinations have been completed, so that their disease may be declared to be a consequence of military service and give them the right to a pension. The physicians take great precautions to detect all fraudulent practices, most of which are well known to them. Considerable improvement has been brought about by the ruling that all conscripts are to be subjected to a thorough radioscopic examination before they are definitely assigned to their unit. Médecin général Rouvillois, in collaboration with Messieurs Christian and Liégeois, reported recently to the Academy of Medicine the first results obtained following the introduction of radioscopic examinations in the army. The idea was first proposed by Médecins généraux Rieux and Sieur, but it took time to procure the technical equipment and the requisite personnel. The results secured confirm the importance of the introduction of this means of investigation. Out of a total of 115,150 recruits examined, 1,093 eliminations were made and final or temporary discharges were granted, representing an average of 9.4 to the thousand, which included 143 persons in whom open tuberculosis was diagnosed. These observations are interesting because they have to do mostly with recruits who had already been accepted at the first examination. The number of cases of tuberculosis detected by systematic radioscopic examination constitutes about one third of the cases detected at the first examination. Following this address, Professor Sergent emphasized the value of this innovation and expressed the hope that the same methods would be applied before persons are allowed to enter any collective group: high schools, universities or even factories. Mr. Béclere took occasion to stress the need of distinguishing types of tuberculosis in an active state from old lesions long since cured.

Noise in the Cities

The steady increase of the external noises today in all large cities has finally begun to attract the attention of hygienists. A crusade against noise has been organized by many municipalities. Almost everywhere one encounters the indifference of the public authorities and the selfishness of the persons responsible for the noises. Some have gone so far as to deny the existence of the nervous disorders produced by noise and to say that noise disturbs only neuropaths and persons who are already ill—who would do well to move into the country. In opposition to such views, Dr. Segard has published a clinical study on what he terms the "Syndrome of Persons Suffering from the Noise Evil." He distinguishes the effects of continuous noises from unexpected noises, which produce a nervous shock, the repetition of which is positively harmful. To the latter class belong noises of gasoline motors, particularly motorcycles and airplanes, loud speakers and phonographs, and the like. A few years ago it was common to compare the irritability of city dwellers to the calmness of villagers. Noises cause nervous disorders. They provoke disturbances of sleep, digestive disorders, irregularity of the pulse and an increase in blood pressure. Dr. Segard stated that the special commission on the noise evil, with headquarters in New York, has estimated that in mental workers this syndrome observed in persons subjected to noises reduces by 20 per cent their working capacity. It is the duty of the municipalities and the responsible authorities to pass regulations controlling the use of automobile horns, locomotive whistles, factory sirens, loud speakers, phonographs and radio sets and to prevent unnecessary noises of vehicles, advise and prescribe the construction of buildings of sound-proof materials, and impose effective penalties for violations of the specifications. It has been proposed that persons troubled by noises at night should put pledgets of absorbent cotton or wax in the ears to reduce the transmission of sound. But such measures are only partially effective and are not without danger. From time to time, persons who are affected by the noises of the city should spend a short period in the country. It would be a good thing if the authorities of certain small cities would make more widely known the measures they have adopted to prevent noise. They would not fail to attract many persons from the large cities who are seeking a quiet place in which to spend their vacation.

BERLIN

(From Our Regular Correspondent)

Aug. 27, 1934.

Heredity and Diseases of the Blood Vessels and Kidneys

Professor Weitz addressed recently the Berlin Medical Society on "Hereditability of Diseases of the Heart, the Blood Vessels and the Kidneys." Congenital cardiac defects are relatively more frequent in certain families and are concordant in dizygotic twins. In one family, pronounced cyanosis could be followed through four generations in seven persons. Numerous necropsy reports refer to similar congenital cardiac defects in siblings. Frequently not only a general predisposition to malformations of the heart are inherited but also even the predisposition to certain definite malformations. The hereditary course may apparently be dominant and recessive.

In acquired cardiac defects, external factors play an essential part. In enzygotic twins, acquired cardiac defects are frequently found to be discordant. A hereditary predisposition must be assumed. Since researches on twins show that a tendency to sore throat is decidedly hereditary, this is doubtless, in many cases, the explanation for the familial aspects of heart defects after endocarditis.

Constitutional cardiac disease is found chiefly in vasoneurotic, infantile and asthenic subjects and in persons with disturbances of the internal secretions. Researches on families and on twins show that vasomotor disturbances, a tendency to extrasystoles and to paroxysmal tachycardia, drop heart and pendulous heart are traceable to hereditary factors.

It has been observed that there are families in which there is a high incidence of the consequences of hypertonia; for example, cerebral hemorrhages. The parents of young hypertonic patients die at an early age from heart disease and cerebral hemorrhage. The hereditary course is in this case dominant.

Alcoholism, mental excitement, immoderate physical exertion and the ingestion of animal protein constitute external factors that serve as precipitating causes in the manifestation of the predisposition. In this connection, interest attaches to investigations on monks. In contrast to monks using a mixed diet, hypertension was seldom found in monks subsisting on a vege-

tarian diet. Arteriosclerosis shows a certain connection with hypertension, and in a heredobiologic study they cannot be entirely separated. Also cerebral arteriosclerosis and angina pectoris have been found to have a familial incidence.

Weitz reports having observed several instances of hypertonia in parents and children. Concordant behavior in enzygotic twins and familial occurrence prove the hereditary nature of thrombo-angiitis obliterans. With respect to varices, family trees have been studied that point unequivocally to a dominant hereditary transmission of the predisposition. In enzygotic twins, varices that occurred were always concordant.

Of the renal diseases one must examine, for three reasons, the hereditability of glomerulonephritis: an increased incidence among siblings following diseases that seldom give rise to nephritis; increased incidence of scarlatinal nephritis in some siblings; increased incidence of nephritis in the family in general.

The cystic kidney in the new-born is probably a recessive hereditary disorder. Cystic kidney in adults, which usually appears beyond the forties in a much more harmful form, seems to have a dominant hereditary course. Since in many cases a cystic kidney is associated with a grave malformation, sterilization is to be considered.

Treatment of Spasm of the Pylorus

In recent years, hypertrophic stenosis of the pylorus in infants has frequently been operated on in accordance with a procedure introduced by Professor Ramstedt of Münster. In 1929 Ramstedt sent a questionnaire to about sixty children's clinics and hospitals for infants to secure information concerning the results of this method. This questionnaire revealed that, during the ten-year period from 1919 to 1928, 1,842 cases of pylorospasm had been treated in the institutions solicited for information. The mortality ranged around 18 per cent, internists reporting a mortality of 16 per cent, while that of cases coming to operation was 22.5 per cent. A recent inquiry of the same nature and extent covers 2,432 cases, with a general mortality of 10.7 per cent, internists reporting a mortality of 9 per cent, while that of cases coming to operation was 14.4 per cent. Thus there has been not only a marked increase in the number of cases but also a gratifying reduction of the mortality in this dangerous disorder. Today this disorder is better diagnosed—more frequently in its beginnings, so that treatment can be begun earlier. Whether the splitting of the hypertrophic pylorus muscle, which Ramstedt recommended, has proved its worth is doubtful, for there is as yet no general agreement as to the indications for operation. The success of surgical treatment makes a better showing if the results of certain clinics that applied only operative methods or only internal methods are compared. In two such series of cases the mortality among 958 infants receiving internal treatment was 10 per cent, and among 1,609 infants receiving surgical treatment, only 8.5 per cent. In the series of cases coming to operation, fifteen pediatricians and surgeons who are advocates of the early operation had an average mortality of only 4 per cent. The children's clinic in Düsseldorf has made a careful comparison. Up to 1928, conservative methods were used exclusively. From 1919 to 1928 the mortality in ninety-two cases was 18.4 per cent; later (1927-1933), when surgical procedures exclusively were employed, the mortality in a series of 110 cases was only 3.6 per cent (four deaths). It would appear that the question has been decided in favor of the operative method. The children treated by operation get well much more rapidly, and they are much less likely to contract intercurrent diseases and infection.

Professor Hertel, surgeon at the University of Münster, expressed himself thus: Up to the present the Ramstedt operation has been performed in twelve cases, in all of which a cure was effected. The age of the patients on the day of the operation ranged between 16 days and 4 months, the average being about 7 weeks. The average duration of treatment was thirty-five days, although in a few instances a child could be dismissed at the end of eleven days. The increase in weight of the infants during this period was about 840 Gm. The vomiting ceased usually immediately after the operation; in some cases it continued several days, being evidently connected with the elimination of the reflex disturbances.

Professor Vogt, ordinarius in pediatrics at the same university, said that the question of choice of method cannot be decided by the scrutiny of statistics, for there is no reason to feel assured that the comparison of the successes is being based on truly comparable cases. Stenoses of the pylorus are sometimes produced by other causes than a simple hyperplasia of the musculature; for example, by changes in the position of the duodenum, with kinking. Experience does not justify the assumption of definite periods within which internal treatment must show good results. In some cases it may take a week and in other cases two weeks or longer before there is a definite turn for the better. Hence progress can be expected only from further research on the dynamics of the various clinical manifestations. In any event, the endeavor to get along with internal treatment without operation is justified primarily by the observations that show the clinical symptoms may disappear permanently in spite of the fact that hypertrophy of the pylorus remains.

Hence, in mild cases, as Ramstedt admits, internal treatment must be tried first, and the pediatrician should select the cases for operation and also determine the time for the operation. That, moreover, the effects of pyloromyotomy are not always immediate is due to the facts that sometimes the muscular hypertrophy along the pyloric ring, which is pushed forward toward the duodenum like a cervix, is especially well developed and that precisely this portion is often difficult to reach with the knife or cannot be divided without danger of opening the duodenum. Such an accident must be avoided without fail.

Diabetes in Jews

Professor H. Strauss, director of the department of internal medicine of the Jewish Hospital in Berlin, has been able to show by mortality statistics that diabetes is of frequent occurrence in Jews. Women are somewhat more frequently affected than men (280:271). The researches on heredity revealed that hereditary influences played a part in 20.6 per cent of the cases in women and 29.7 of the cases in men. The hereditary influence manifests itself usually in a recessive form. A large majority of the patients were merchants. That wealth exerts a decided influence could not be demonstrated. More than three fourths of the cases were moderate or mild. In a large number of cases, only diabetes innocuus was involved. In 20 per cent of the cases the duration of the disorder extended over eight years or more. Polydipsia as a beginning symptom was demonstrated in men in 46 per cent and in women in 40 per cent of the cases. Pruritus was an associated disorder in 27.5 per cent of the women. Furunculosis was more frequent in men than in women. Gangrene of the extremities was found in 7 per cent of the men and in 5 per cent of the women. In the opinion of Strauss, the real frequence of diabetes in the Jews is due to hereditary influences and to increased lability of the vegetative nervous system.

The Health of School Children

In 1925 Professor Czerny and Professor Keller, pediatricians of Berlin, reached the conclusion that the damage to the development and the health of children caused by the war period was less than was expected. The economic crisis in 1930 and the increasing unemployment have awakened renewed interest in the matter. Also the League of Nations has studied the question of "Economic Crises in Relation to Public Health." Examination of school children in later years did not reveal

harmful late effects of war conditions. A change occurred, however, in 1933, for health conditions among the youth took a turn for the worse last year. Many different types of infectious disease appeared in the districts controlled by school physicians—often in an unusual form. Of decisive significance, as Professor Keller points out, was the condition discovered in the children who entered school for the first time in February 1934. The entrance examination revealed the wretched bodily condition of the children born in the years 1927 and 1928. Many of these children gave evidence of very poor nutrition and a poor constitution. A normal set of teeth was rare, and it was evident that they lacked adequate resistance toward disease. Hence special welfare measures must be applied to these children, and they must receive supplementary food allowances for the first few months of school life. Physicians engaged in social work should determine the extent of this impaired condition of health among school children and endeavor to remedy conditions as promptly as circumstances will permit.

Personal

Prof. Kurt Schneider of Munich has received a call to the chair of psychiatry, as the successor of Prof. W. Weygandt (retired), in Hamburg.

Prof. Erich Hoffmann, ordinarius for dermatology at the University of Bonn, has been relieved of his official duties and has been appointed an outside member of the Georg Speyer-Haus in Frankfort-on-Main.

Prof. S. J. Thannhauser, ordinarius for internal medicine in Freiburg-im-Breisgau, has been retired by reason of the new legislation pertaining to officials. Professor Bohnenkamp of Giessen has been appointed his successor and will serve also as director of the University Medical Clinic.

Professor Jacobsthal of Hamburg has been called to the University of Guatemala as professor and director of the Bacteriologic Institute.

Dr. H. Löhr, superintendent of the Bethel Hospital, near Bielefeld, has been appointed ordinarius for internal medicine at the University of Kiel, to succeed Professor Schittenhelm, who has been called to the University of Munich.

Professor Nonnenbruch of Prague has declined a call to the chair of internal medicine in Hamburg, as the successor of Prof. L. Brauer, retired.

Prof. Otfried Müller, director of the University Medical Clinic in Tübingen, has been relieved of his official duties because of illness.

Dr. R. Fetscher, extraordinary professor of eugenics and biology as pertaining to heredity, at the Dresden Polytechnicum, has been retired by reason of the new legislation.

Prof. F. Dessauer, radiologist and ordinarius for medical physics at the University of Frankfort-on-Main has been retired by reason of the new legislation.

Professor Broemser of Heidelberg has accepted a call to the chair of physiology at the University of Munich.

Prof. Heinrich Braun, formerly director of the infirmary in Zwickau, has died at the age of 71. Braun performed meritorious service in the development of local anesthesia and is the author of a textbook on this subject.

Prof. P. Mühlens of Hamburg has been appointed director of the Hamburg Institut für Schiffs- und Tropenkrankheiten, in which he had been serving as department director. He has likewise become ordinarius in tropical medicine at the University of Hamburg.

Prof. Dr. Paul Krause, ordinarius in internal medicine in Münster (Westphalia), is a suicide at the age of 62.

Prof. Dr. Heinrich Eymer of Heidelberg has accepted a call to the chair of gynecology at the University of Munich, as the successor of Geheimrat Professor Doederlein, retired.

Prof. Dr. Gustav Aschaffenburg, psychiatrist and ordinarius of Köln, has been relieved of his official duties.

RIO DE JANEIRO

(From Our Regular Correspondent)

Aug. 15, 1934.

Malignant Diphtheria

Drs. Jose M. da Rocha, pediatrician of the Hospital São Sebastião, and Clarindo Rabello, intern of the hospital, reported before the Society of Pediatrics a case of malignant diphtheria in a child, aged 9 years, which died in four days. Necropsy revealed punctiform hemorrhages in the skin and mucosae and hemorrhages in the lungs, kidneys, heart, peritoneum and stomach. They had injected 100,000 units of antidiphtheritic serum, of which 20,000 was given intravenously. Cases of hemorrhagic malignant diphtheria are rare in Rio de Janeiro but they have become more frequent lately. The authors reviewed the various theories on the causes of malignant diphtheria: bacterial association, virulence, toxicity of the germs and toxins, and constitutional factors. They came to the conclusion that the factor of greatest importance is a constitutional predisposition to hemorrhages.

Roentgenkymography of Aortic Aneurysms

Dr. J. M. Cabello Campos, roentgenologist of the Sanitary Service of Santa Casa and of the Institute of Hygiene of São Paulo, presented to the Society of Medicine and Surgery some work on roentgenkymography. He enumerated the difficulties encountered in practice in diagnosing tumors of the mediastinum, particularly aneurysms, in which the relations of the tumor mass to the artery and its movements are valuable signs. After giving an outline of the technic employed and a description of the apparatus in use, he reported in detail the kymographic curves of four cases of aneurysm. Roentgenkymography is indispensable in the differential diagnosis of tumors of the mediastinum.

VIENNA

(From Our Regular Correspondent)

Aug. 23, 1934.

Arteriosclerosis in Vienna

Addressing recently the Vienna Medical Society, Dr. Fellner reported his observations on 12,000 patients with arteriosclerosis. His research considered the degree and the dissemination of sclerosis in the aorta, the coronary vessels, the vessels of the brain, and the remaining large arteries. It was found that, as a rule, women contract the disease later than men and present a milder type. Not until the age of 70 is reached are the curves for the two sexes approximately the same. One finds, however, fatty degeneration of the vessels more frequently in women. Calcification begins with the arteries of the brain after the age of 35, and from 10 to 15 per cent of the 70-80 age group give distinct evidence of this condition. The heart vessels are calcified in about 50 per cent of the persons belonging to the age groups above 60. A difference between the calcification of the aorta and the remaining vessels is seen only in inveterate smokers. Thirty per cent of the latter give distinct evidence of calcification of the peripheral vessels. The aorta and the heart vessels are more frequently calcified in persons of stocky build than in persons of a more athletic type; the latter, however, often present sclerotic heart vessels. Obese persons show a tendency to fatty degeneration of the vessels—obese women particularly. Sclerosis appears earlier and more frequently in Jews than in the average population. In the rural population, the disease develops later and in a milder degree. Social factors appear to play a part. The well-to-do classes are inclined to live a sedentary life and doubtless ingest more toxins in their diet; hence arteriosclerosis appears earlier in this class. The same thing is true of mental workers. In the latter class, however, not the brain but the aorta is attacked

earlier and more severely. Severe physical labor that is combined with considerable movement does not predispose a person to early sclerosis; but if the severe labor is done in a standing position with little movement (porters, laundresses), arteriosclerosis develops early. Alcohol addicts are no more predisposed to arteriosclerosis than are abstainers. Excessive use of tobacco, however, plays havoc with the blood vessels. Tuberculosis has no effect on the blood vessels, whereas syphilis produces grave changes, particularly in the ascending aorta. Rheumatism and carcinoma appear to have no influence on the vessel walls, although diabetes is frequently associated with early and severe arteriosclerosis. Gallstones and liver disorders frequently produce fatty degeneration of the vessels.

The Population of Vienna

On March 22, 1934, a census of Austria was taken, the preliminary results of which have been published. The population of Vienna is given as 1,874,618, which is a loss of 142,000 as compared with 1914. The total number of living births for 1913 was 12,137, and the total number of deaths was 23,472. In 1914 there were more than 26,000 births, which shows a decline of more than 50 per cent, over against 22,000 deaths. The excess of deaths over births, amounting in 1933 to 11,335, was counterbalanced by immigration. The total number of immigrants was 155,587, over against an emigration of 122,443, so that, in spite of the declining birth rate, the population had increased by 21,809. For the first quarter of 1934 the number of living births was 3,368; the number of deaths, 6,642; the number of immigrants, 35,426, and the number of emigrants, 30,019, so that the net increase in population for the first quarter of this year was 2,133.

The statistics for the Jews of Vienna are interesting. In 1914, and also in 1934, the Jews constituted about 10 per cent of the total population (200,000 and 178,000 respectively). The decline in the birth rate among the Jews (60 per cent) is possibly even greater than among the non-Jewish population, but the mortality is somewhat lower. There were no Jewish immigrants, and the emigration was small, although the last two years have shown an increase. An evident fact, however, is the constant distinct decrease in the Jewish portion of the population since 1920. From a total of 218,000 in 1918, the Jewish population has dropped to 178,000, signifying a loss of 40,000, or almost 20 per cent of the maximum.

A Study of Abortion

Professor Zacherl and Dr. Richter of the Innsbruck Geburtshilfliches Universitäts-Institut reported to the Austrian public health service on their research on the sequels of abortion. All statistical reports reveal a marked increase of abortion, since the war, among all civilized nations. It was found that the immediate damage resulting from abortion, such as death and inflammatory processes, is of less significance, on the whole, than the late results affecting the health of the woman and her fertility. The damage due to abortion may be considered under three heads: hemorrhages, infections and anatomic injuries. The speakers reported the results of their observations in a series of 2,000 gravidas in Innsbruck. The majority of the women presented after abortion various disorders of genital origin. Menstruation was much disturbed in more than 50 per cent, while amenorrhea was a frequent symptom. In a large number of cases, sterility was later demonstrable; likewise, anatomic changes in the genitalia were observed in many cases. Later births, and even pregnancies, are more likely to show complications than in women who have never had an abortion. Placenta praevia is especially frequent; likewise, weak labor pains are common, and prolongation and disturbance of the after-birth period. Death of the fetus before the end of term, habitual miscarriage and febrile births are relatively more frequent in such women. Both speakers expressed the view that a large part of the late injuries following interruption of pregnancy are due to errors of technic. They recommend, therefore, a very conservative operative method in abortion and conservative after-treatment—methods that take careful account of the physiologic conditions. A common error of technic is the too radical removal of the uterine mucosa. The resulting inadequate regeneration produces a functional inferiority of the mucosa, with the aforementioned consequences, and also leukorrhea, chronic inflammations, disturbance of nidation of the ovum, and the frequently observed secretory, hormone disturbances.

Conflict Between the Vienna Faculty of Medicine and American Students

A controversy that threatened to destroy the friendly relations between the Vienna Faculty of Medicine and the medical students from America studying in Vienna was settled at the last moment by the intervention of the American ambassador to Austria and the Austrian ministry of public instruction. The controversy arose over the selection of courses of study designed for foreigners, which are largely attended by Americans. The society of American medical students bearing the name "American Medical Association of Vienna" has functioned satisfactorily for about thirty years. The society established, some years ago, its own committee for the selection of the courses to be given by English-speaking Vienna professors. It goes without saying that, in the selection of these courses, the wishes of the Americans, who were in the majority, received the chief consideration. The Vienna Faculty of Medicine has also its committee to decide what courses shall be given in the German language. For various reasons the attendance on these courses has been, in recent months, much reduced. In order to improve the attendance on its own courses, the committee of the Faculty of Medicine attempted to deprive the American Medical Association of Vienna of the right to organize its own (English) courses. Doubtless, certain political factors played a part in the controversy; for, in the Faculty of Medicine, there was evidence of influence traceable to the national-socialists. There seemed to be a movement to allow certain physicians the privilege of holding medical courses in English, but, at the same time, an endeavor was made to withhold this source of income from Jews.

In other words, the committee on courses of the Faculty of Medicine desired to furnish the association not only the courses but also the lecturers, without giving much consideration to the wishes of the students themselves. The proposal was rejected by the American physicians as being untenable, and they even went so far as to threaten to leave Vienna in a body if they were to be denied the privilege of selecting their own courses. In spite of this, the Faculty of Medicine, under the influence of political agitators, refused to yield. Thereupon the president of the association entered into correspondence with the universities of Prague and Budapest, which expressed a willingness to meet the requirements of the foreign physicians, in order to induce them to move to their city. The American ambassador in Vienna was informed of the situation, and he took up the matter with the ministry of public instruction. At last a way had been found to effect a solution of the difficulty. The ministry of public instruction issued an order that the selection of courses for the American physicians be continued to be made as in the past. By the events in July, which took the form of a Nazi revolt, the disturbing agitators in the Faculty of Medicine were eliminated, so that it appears likely that the differences between the Faculty of Medicine and the foreign medical society of Vienna will soon be settled and that the medical school of Vienna will retain its age-old position as a center for medical education.

Marriages

JUNIUS HAZEL MCLEOD, Fayetteville, N. C., to Miss Waverly Gwynne Thomas of Smithfield, Va., August 5.

LINVILLE MURRELL HALLORAN, Beckley, W. Va., to Miss Frances Louise Williams of Lexington, Va., August 31.

ROBERT LUCIEN MCCOLLOM, Flushing, N. Y., to Miss Virginia Muir of St. Albans, September 21.

MALACHI WILSON SLOAN JR., Berrysburg, Pa., to Miss Ellen Kathryn Wisler of Norristown, August 11.

FREDERICK EARL MCLENDON, Athens, Ga., to Miss Bennie Venetta Bell of Nashville, Tenn., June 27.

RAYMOND L. CLATERBAUGH to Miss Louise H. Scruggs, both of Clifton Forge, Va., September 8.

JAMES F. CASTO, Topeka, Kan., to Miss Lorane Carder of Lawrence at Wellsville, September 9.

OSCAR ADOLPH KAFER, Winston-Salem, N. C., to Miss Helen Elizabeth Seifert, September 24.

EMMETT A. DOLES, Havre, Mont., to Miss Claremae Vielleux of Fort Benton, September 29.

OSCAR LEE HITE, Richmond, Va., to Miss Inez De Jarnette of South Boston, September 22.

EDWARD CHARLES MAEDER, Minneapolis, to Miss Irene Kangas of St. Paul, July 24.

JAY MCLEAN, New York, to Miss Georgia Alpin of Fayetteville, N. C., June 5.

FRANCIS W. BRIGGS to Mrs. Agnes Lamey, both of Havre, Mont., recently.

Deaths

Curran Pope ⊕ Louisville, Ky.; University of Louisville School of Medicine, 1889; member of the House of Delegates of the American Medical Association in 1912; past president of what is now known as the American Congress of Physical Therapy and the Ohio Valley Medical Association; member of the American Psychiatric Association and the Kentucky Board of Charities and Corrections; lecturer on pathology, bacteriology and microscopy, Hospital College of Medicine, 1891-1894; professor of neurology and psychiatry, Louisville College of Medicine, 1895-1899; adjunct professor of neurology, psychiatry and physical therapy, Kentucky School of Medicine, 1902-1908, and professor of physical therapy at his alma mater, 1909-1910; consulting neurologist and psychiatrist to St. Anthony's Hospital; medical director of a hospital bearing his name; author of "Practical Hydrotherapy"; aged 67; was found dead, September 21, of a self inflicted bullet wound.

Arthur Percival Procter, Vancouver, B. C.; Canada; Manitoba Medical College, Winnipeg, 1896; for twenty-two years registrar of the College of Physicians and Surgeons of British Columbia; for twenty-five years chief medical officer of the Canadian Pacific Railway for the British Columbia division; for seventeen years district medical officer department of pensions and national health, Shaughnessy Military Hospital; aged 67; died, August 20, of a gunshot wound.

Guy Edmund Manning, San Francisco; Hahnemann Medical College and Hospital of Philadelphia, 1890; at one time librarian, professor of materia medica, physiology and chemistry, Hahnemann Medical College of the Pacific; for many years member of the city board of health; health commissioner of San Francisco, 1907-1921; director of the Hahnemann Hospital, 1910-1918; aged 67; died, September 1, of cerebral thrombosis.

Edward Ernest Maxey, Aberdeen, Wash.; College of Physicians and Surgeons of Chicago, 1891; member of the Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; served during the World War; past president and secretary of the Idaho State Medical Society; on the staffs of St. Joseph's and Aberdeen General hospitals; aged 67; died, August 31, of coronary occlusion.

Fellowes Davis Jr., New York; Columbia University College of Physicians and Surgeons, New York, 1899; served during the World War; formerly on the staff of the New York Nursery and Child's Hospital; governor of the American Hospital, Neuilly, France; aged 62; died, September 5, at his summer home in St. James, L. I., of adenocarcinoma of the prostate.

Clarence Ruter Dufour, Washington, D. C.; Howard University School of Medicine, Washington, 1889; Georgetown University School of Medicine, 1890; member of the Medical Society of Virginia; formerly emeritus professor of clinical ophthalmology, Georgetown University School of Medicine; aged 71; died, September 11.

Richard Charles Weithas ⊕ Brooklyn; George Washington University Medical School, Washington, D. C., 1909; member of the American Urological Association; fellow of the American College of Surgeons; urologist to the Bushwick and Coney Island hospitals; aged 51; died suddenly, September 27, of heart disease.

John Milton Garrett ⊕ Fort Dodge, Iowa; Marion-Sims College of Medicine, St. Louis, 1892; Bellevue Hospital Medical College, 1896; past president and secretary of the Webster County Medical Society; on the staffs of the Lutheran and St. Joseph Mercy hospitals; aged 65; died suddenly, August 18, of heart disease.

Edward Montraville Swift ⊕ Perth Amboy, N. J.; Howard University School of Medicine, Washington, D. C., 1927; on the staff of the Perth Amboy General Hospital; aged 47; died, September 9, in the Mount Sinai Hospital, New York, of malignant hypertension, uremia and heart disease.

Jacob H. Mitnick, Baltimore; Baltimore Medical College, 1890; member of the Medical and Chirurgical Faculty of Maryland; veteran of the Spanish-American and World wars; aged 76; died, September 22, of arteriosclerosis, diabetes mellitus and coronary thrombosis.

Samuel Pilgrim Gerhard ⊕ Philadelphia; Medico-Chirurgical College of Philadelphia, 1891; Jefferson Medical College of Philadelphia, 1893; formerly lecturer on medicine, Temple University School of Medicine; aged 67; died, September 8, of heart disease.

Cornelius DeWeese ⊕ Washington, D. C.; Jefferson Medical College of Philadelphia, 1895; member of the American Psychiatric Association; medical director of the Laurel Sanitarium, Laurel, Md.; aged 59; died suddenly, September 15, of cerebral hemorrhage.

James Arthur Kirk, Danville, Ill.; Hospital College of Medicine, Louisville, Ky., 1904; served during the World War; aged 53; on the staff of the Veterans' Administration Facility, where he died, September 3, of Hodgkin's disease and chronic pulmonary tuberculosis.

George Enos Burdick, Hines, Ill.; University of the City of New York Medical Department, 1888; served during the World War; on the staff of the Veterans' Administration Facility; aged 69; died suddenly, September 24, in Glen Ellyn, of coronary occlusion.

Marvin Whitfield Glasgow, Fairfield, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1901; aged 56; on the staff of the Employees' Hospital of the Tennessee Coal, Iron and Railroad Company, where he died, September 20, of heart disease.

Antoine Paul Cartier, St. Hyacinthe, Que., Canada; School of Medicine and Surgery of Montreal, Que., 1872; formerly conservative member of the Quebec Legislative Assembly for the County of St. Hyacinthe; aged 85; died, July 10.

William N. Gilmore ⊕ East Liverpool, Ohio; Western Reserve University Medical Department, Cleveland, 1882; on the staff of the East Liverpool City Hospital; aged 76; died, August 29, of cerebral hemorrhage and arteriosclerosis.

Louis Nels Andersen ⊕ Inglewood, Calif.; College of Physicians and Surgeons, Medical Department Kansas City (Kan.) University, 1896; served during the World War; aged 70; died suddenly, September 6, of heart disease.

John Alva Longmore ⊕ Brooklyn; University of Michigan Medical School, Ann Arbor, 1900; formerly lecturer in medicine and chief of the clinic, Long Island College Hospital; aged 59; died, September 13, of heart disease.

Francis Bernard Conway, Boston; Tufts College Medical School, Boston, 1903; member of the Massachusetts Medical Society; aged 64; died, September 10, in the City Hospital, of coronary thrombosis and bronchopneumonia.

John Philip Dougherty ⊕ Sioux City, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, Chicago, 1904; aged 59; died, August 18, following an operation for gallstones.

Belmont De Forest Bogart, New York; Columbia University College of Physicians and Surgeons, New York, 1896; aged 62; died, September 8, in the Hospital for Ruptured and Crippled, of hypertensive heart disease.

Bernard M. Turbow, East Chicago, Ind.; Chicago College of Medicine and Surgery, 1913; member of the Indiana State Medical Association; aged 48; died, October 2, at his home in Indiana Harbor, of coronary thrombosis.

Caesar A. Queirolo, Oakland, Calif.; Université de Genève Faculté de Médecine, Genève, Switzerland, 1897; aged 65; died, July 18, in the Providence Hospital, of carcinoma of the pleura with abdominal metastasis.

John Rogers Parry ✠ Woodsfield, Ohio; Medical College of Ohio, Cincinnati, 1878; formerly secretary of the Monroe County Medical Society; aged 79; died, August 29, of chronic myocarditis and arteriosclerosis.

Frank Lydston Newman, Detroit; Detroit College of Medicine, 1887; formerly emeritus professor of pharmacology and therapeutics at his alma mater; aged 74; died, August 23, of uremia and chronic nephritis.

Archibald Williamson, Richmond Heights, Mo.; Beaumont Hospital Medical College, St. Louis, 1889; aged 68; died, July 25, in the Evangelical Deaconess Home and Hospital, St. Louis, of carcinoma of the pancreas.

John Harrison Wedig ✠ Wood River, Ill.; Chicago College of Medicine and Surgery, 1910; served during the World War; aged 49; died, September 7, in St. Joseph's Hospital, Alton, of sarcoma of the lung.

Oscar Beesley Dunn, Ironton, Ohio; Miami Medical College, Cincinnati, 1878; member of the American Academy of Ophthalmology and Oto-Laryngology; aged 84; died, September 11, of myocarditis.

Jesse Bell Porter, Fort Myers, Fla.; Northwestern University Medical School, Chicago, 1903; aged 62; died, August 1, in a hospital at Miami, of bronchopneumonia following bilateral herniotomy.

Stanislaus A. Kulick ✠ Detroit; Michigan College of Medicine and Surgery, Detroit, 1896; aged 59; died suddenly, September 5, at his summer home in Fair Haven, Mich., of cerebral hemorrhage.

Horace Greely Pangle, Russellville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1898; aged 61; died, September 6, in a hospital at Greenville, of diabetes mellitus and heart disease.

Henry Burton Parrish, Nashville, Tenn.; University of Tennessee Medical Department, Nashville, 1904; served during the World War; aged 55; died, September 23, in the Protestant Hospital.

Jefferson Woolsey, Karnes City, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1894; served during the World War; aged 64; died, July 26, of cerebral hemorrhage.

Joseph Edward Pelletier, Worcester, Mass.; School of Medicine and Surgery of Montreal, Que., 1903; aged 58; died, August 7, of arteriosclerosis, coronary sclerosis and auricular fibrillation.

Llewellyn C. Kellogg ✠ Loma Linda, Calif.; College of Medical Evangelists, Los Angeles, 1922; professor of anatomy at his alma mater; aged 58; died, September 1, of coronary occlusion.

Clement Emerson Sayers, Hawthorn, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1896; member of the Medical Society of the State of Pennsylvania; aged 66; died in June.

William Bidwell Page, Denver; University of Michigan Homeopathic Medical School, Ann Arbor, 1883; aged 77; died, September 2, of arteriosclerosis, coronary sclerosis and myocarditis.

Milton S. Gray, Phoenix, Ariz.; Ensworth Medical College, St. Joseph, Mo., 1896; member of the Missouri State Medical Association; aged 64; died, September 8, of heart disease.

Nolan Ray Currie, Jackson, Miss.; Birmingham (Ala.) Medical College, 1909; member of the Mississippi State Medical Association; aged 51; died, September 4, of heart disease.

George William Flynn, St. Louis; St. Louis University School of Medicine, 1910; member of the Missouri State Medical Association; aged 48; died, August 23, of heart disease.

Marie McGarvey Peake, Blair, Neb.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1900; aged 68; died, August 26, of polyneuritis and inanition.

Dale L. Walker, St. Clairsville, Ohio; Jefferson Medical College of Philadelphia, 1885; aged 73; died, September 8, in Columbus, of cerebral hemorrhage and arteriosclerosis.

Alwin Meigs Guittard, Cabanatuan, P. I.; Cleveland College of Physicians and Surgeons, Medical Department of the University of Wooster, 1885; aged 74; died, July 14.

John Andrew Podsedly, Cleveland; St. Louis University School of Medicine, 1926; aged 34; died, August 9, in the Cleveland Clinic Hospital, of a pontile tumor.

George Oliver Gernon, Ste. Geneviève de Pierrefonds, Que., Canada; University of Bishop College Faculty of Medicine, Montreal, 1879; aged 80; died, July 1.

Jacob Kurnik, Brooklyn; Long Island College Hospital, Brooklyn, 1914; aged 46; died, August 26, in the Worrell Hospital, Rochester, Minn., of pemphigus.

Harry Lee Bell ✠ Knox, Ind.; Chicago College of Medicine and Surgery, 1908; served during the World War; aged 56; died, August 7, of acute myocarditis.

Timothy Charles Weber, West Salem, Ill.; Barnes Medical College, St. Louis, 1897; served during the World War; aged 64; died, August 28, of tuberculosis.

Aaron P. Baldwin, Tyler, Texas; Louisville (Ky.) Medical College, 1883; aged 76; died, July 10, of hepatitis, cholecystitis, myocarditis and chronic nephritis.

Julius H. Krueger, Chicago; Hahnemann Medical College and Hospital, Chicago, 1887; aged 88; died, September 25, of cerebral hemorrhage and arteriosclerosis.

Ida Leonora Schell ✠ Milwaukee; Northwestern University Woman's Medical School, Chicago, 1900; aged 71; died, September 21, of cerebral hemorrhage.

Albert M. Phillips, Eulogy, Miss.; University of Tennessee Medical Department, Nashville, 1887; aged 69; died, August 30, of cerebral hemorrhage.

Henry Jakob Strauch, Donora, Pa.; Jefferson Medical College of Philadelphia, 1928; aged 42; died, September 8, in the *Morro Castle* disaster.

James Patrick Coll, Jersey City, N. J.; Jefferson Medical College of Philadelphia, 1904; aged 51; died, September 8, in the *Morro Castle* disaster.

Charles Bloodgood; Grand Rapids, Mich.; Rush Medical College, Chicago, 1881; aged 81; died, September 7, of a self inflicted bullet wound.

Walton Worthey Shoemaker, Handley, Texas; Medical College of Alabama, Mobile, 1892; aged 77; died, July 26, in a hospital at Fort Worth.

William Erastus Wells, Tampa, Fla.; University of Louisville (Ky.) School of Medicine, 1901; aged 58; died, July 15, of dilatation of the heart.

James E. G. Simmons, Boyd, Texas; Atlanta (Ga.) Medical College, 1888; served during the World War; aged 74; died, July 26, of senility.

Albert James Storm, Collingdale, Pa.; Medico-Chirurgical College of Philadelphia, 1915; served during the World War; aged 46; died, July 14.

George Wilson Bass, Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1890; aged 71; died, August 23, of arthritis.

Samuel Sal Murnick, Chicago; Loyola University School of Medicine, Chicago, 1922; aged 40; died, September 16, of organic heart disease.

Felix Jasper Bray, Parsons, Tenn.; Vanderbilt University School of Medicine, Nashville, 1878; aged 80; died, August 29, of prostatitis.

Walter Gustavus Rundle, Lincoln, Neb.; Rush Medical College, Chicago, 1906; aged 58; died, September 10, of cerebral hemorrhage.

James M. Amiss, Silver Lake, Ind.; Medical College of Indiana, Indianapolis, 1880; aged 82; died, September 6, of hemiplegia.

Frank Songer, Hillsboro, Ind.; Medical College of Indiana, Indianapolis, 1891; aged 68; died, September 23, of chronic nephritis.

Walter Myers Gill, Dormont, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1888; aged 69; died, July 12.

Ralph Moore Peters, Minneapolis; Rush Medical College, Chicago, 1894; aged 62; died, August 12, of coronary thrombosis.

Eleanor Stallard Dailey, Omaha; Woman's Hospital Medical College, Chicago, 1878; aged 80; died, June 26.

Richard Gantz, Terre Haute, Ind. (licensed in Indiana in 1897); aged 89; died, September 7, of pneumonia.

Correspondence

THE INTRAVENOUS DRIP

To the Editor:—There appears to be some controversy as to priority in the use of the intravenous drip. I have been intensely interested in intravenous therapy during the past thirty years.

Dr. Rudolph Matas read a paper on "Continued Intravenous Drip" at a meeting of the American Surgical Association held at Rochester, Minn., in 1923, which was published in the transactions of the association for that year and in the *Annals of Surgery* (**79**:643 [May] 1924). In that paper he reported cases in which he applied the method as far back as April 1913 and even before that date. It was my pleasure to observe the use of the continuous intravenous drip under Dr. Matas's service while visiting the Touro Infirmary and Charity Hospitals, New Orleans, in January 1914. It has been in current use in these institutions since 1923, where it is usually designated as the "Matas drip."

Dr. G. A. Hendon of Louisville, Ky., has published a number of papers on the same procedure, under the title of "venoclysis." In a paper which he read at a meeting of the Southern Surgical Association in 1929 (*Transactions* **42**:288, 1929) he says: "On May 12, 1924, I first employed the method," and again, "in June 1924, as a result of a paper on the continuous intravenous drip by Dr. Rudolph Matas, read before the American Surgical Association in June 1923. The paper was published in the *Annals of Surgery* for May 1924."

This acknowledgment from Dr. Hendon himself should suffice to settle the question of priority so far as he is concerned. The only difference is in the name "venoclysis," which he applied to the continued intravenous drip. This has been severely criticized by Cutting and others as a philologic barbarism, because it is a hybrid of Latin and Greek. Matas frequently referred to "phleboclysis" long before Hendon thought of "venoclysis," but even though "phleboclysis" is not so objectionable to philologic purists, it does not convey the notion of the continuance and duration of the procedure. The Greek "phleps" and "klysis" mean, literally, no more than a flushing out or washing of the vein, which is not strictly applicable to any intravenous injection. Although I am not so meticulous about words, I do believe that whoever attempts neologism, especially in scientific matters, should be, at heart, consistent and respectful of philologic rules.

In the Louisville *Courier Journal* of March 2, 1933, Hendon apparently claims to be the originator of the continued intravenous drip. Despite his admission that the practice of "venoclysis," as he calls it, was suggested to him by Matas's paper of 1924, his claim would appear somewhat belated.

In Germany, Friedmann of Langersdreer is recognized as the originator of the method, which he described for the first time at the meeting of Rhenira and Westphalian surgeons at Düsseldorf, Feb. 16, 1913. He then used salt solution for continuous instillation in the veins, from eight to twenty-three hours, reinforcing it with epinephrine, digitalis, and other drugs. This is an important historical event, because there has been some talk recently in Germany of celebrating the twenty-first anniversary of Friedmann's valuable innovation.

I believe there is no question that Friedmann is the first to have introduced the continued drip in Germany, just as I am confident that Matas was the first to use and publish a report of his experience with it, independently, in this country, without knowledge of Friedmann's work.

The records of Matas (as shown in his paper of 1924) go back to April 1913, therefore antedating the first publication of Friedmann's work in the *Zentralblatt für Chirurgie*, Dec. 6, 1913.

The first report ever made on intravenous infusion at the Charity Hospital of New Orleans, from June 1889 to June 1891, was published by Matas. This covered every case in which intravenous infusions had been resorted to in that institution during that period. The report appeared in two issues of the *New Orleans Medical and Surgical Journal* **19**:1-22, 81-33, 1891. For this reason it is easy to understand that with this background of experience the value of the continued drip should have gradually suggested itself.

As to Cutting and his paper on the "Place of Phleboclysis in Surgery," which appeared in the *New Orleans Medical and Surgical Journal* for July 1933, it has nothing to suggest any discussion of history or questions of priority. It is a good review of the actual status of the question, with special stress on some debated new features, which had developed from 1923 to 1932, but there was no pretense at original discovery on the fundamentals.

W. FOREST DUTTON, M.D., Amarillo, Texas.

Queries and Minor Notes

ANONYMOUS COMMUNICATIONS and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted, on request.

HYPERSENSITIVITY

To the Editor:—I had severe asthma in my teens. It completely subsided after a cautery of what was said to be a hypertrophied inferior turbinal. I have not recently been altogether free from trouble. I have put it down to a reflex nasal cause, as cauterization of the nose relieves me for a while. My nasal mucosa too is extraordinarily sensitive to dust, chill and so on. I have noticed that it registers by immediate flow of secretion and sneezing on the slightest exposure to cold of any part of my body on a cold night. On a recent occasion the rhinologist had considerable difficulty in cocainizing my nose, as I sneezed out every cocaine plug he put in prior to cauterization. Recently I had occasion to take a dose of antitetanic serum after a minor accident. As I had taken antitetanic serum two years before, I anticipated trouble because of my asthmatic history. Desensitization was started with a drop of undiluted serum. It raised a wheal and was followed by a few urticarial patches. Two more intradermal instillations of a drop each gave similar patches confined to the ipsilateral arm. Next day I had a frightful, widespread eruption of urticarial patches all over the body, not easily amenable to injections of epinephrine, intravenous calcium gluconate, dextrose, spirit of ammonia and ephedrine by mouth and saline purgatives. The urticaria subsided slowly in the course of the day. My blood showed no eosinophilia. I have since taken graded doses of antitetanic serum up to 1 cc. after testing with drop doses of diluted serum. All the doses gave local reactions in the shape of more than usual pain and hot swelling for two days. I should be obliged to you for information on (1) whether it is possible to desensitize my nose against the extraordinary sensitiveness to cold and (2) whether my "desensitization" against serum will be permanent. If not, is there any method of permanent desensitization? Please omit name and address.

M.D., India.

ANSWER.—The inquirer has hyperesthetic rhinitis and asthma, both probably of allergic origin. The early onset of the asthma, the associated rhinitis and the sensitiveness to horse serum are the prominent factors that speak for an allergic cause. The repeated temporary relief of the asthma following the use of the cautery in the nose does not justify the stamping of the asthma as reflex. Cauterization of the tonsils, tonsillectomy, a nasal operation, an appendectomy, a herniotomy or any procedure that traumatizes tissue or produces a hemorrhage may result in temporary relief of any allergic manifestation. This is due to the nonspecific effect of the absorbed organic matter.

Physical allergy to cold does exist as a primary phenomenon without concomitant allergy to chemical substances such as foods, pollens and animal danders. It must be recognized, however, that physical factors usually operate as secondary causes. Thus, perhaps the majority of instances of hyperesthetic rhinitis have attacks precipitated by physical (heat or cold), chemical (vapors, fumes), mechanical (inorganic dust), infections and neurogenic factors. And yet in most of these cases an underlying chemical allergy is present, which, if removed, will no longer be influenced by the secondary causes.

1. Whether a secondary or a primary factor, it is possible to gain a tolerance to cold. One method consists of taking daily baths, beginning with a temperature well above the point at which symptoms are usually produced and diminishing it by about 1 degree Fahrenheit every two or three days. After

a fairly low temperature is reached, tolerance may be maintained by daily cold baths. Another plan that may be pursued consists of a hot bath or exposure to a therapeutic lamp followed by a rub down with ice, followed again by exposure to heat.

2. Desensitization against horse serum in a sensitive individual to a degree that will allow him to take the usual amount of therapeutic or prophylactic serum is extremely difficult and almost impossible. Whatever "desensitization" or hyposensitization is accomplished is not permanent. The rapid method of attempting to gain a tolerance to horse serum in the space of a few hours is to be condemned not only for its lack of success but because of its great danger. It is important in this connection to differentiate between the naturally horse-sensitive individual and the one who has acquired sensitiveness to serum by a previous injection. In the latter type the degree of sensitiveness is usually much milder than in the first. If there is a history of asthma or rhinitis when the individual is around horses he may be, but is not necessarily, sensitive to horse serum. It is particularly in the latter type that serious and fatal reactions occur from the administration of horse serum.

It is perfectly possible that horse dander may play a part in the causation of the inquirer's asthma and rhinitis. Such dander could have its origin in the horsehair of mattresses or furniture and in the dust of the street, boulevards and parks, in which horse manure, mixed with horsehair, is used frequently for fertilizing and protective purposes. A more detailed discussion of the problem of horse dander and horse serum may be found in S. M. Feinberg's Allergy in General Practice (Philadelphia, Lea & Febiger, 1934, pp. 72, 152 and 154).

If the inquirer has not already done so he should test himself with various allergens, including horse dander, and, if he is found sensitive to the latter, treatment with extracts of horse dander would probably be advisable.

APPENDICITIS OR PYELITIS WITH OTITIS MEDIA

To the Editor:—About three weeks ago I was called to see a girl, aged 6 years, who complained of severe pain over McBurney's point. There was distinct rigidity over the rectus muscle, a temperature of 103 F. by rectum and a differential count of 84 per cent polymorphonuclears with a total count of 17,500 white cells. A surgeon confirmed the diagnosis of acute appendicitis and recommended operative intervention. The parents hesitated and requested me to call in a medical man. By the time the latter arrived the temperature had dropped over 2 points, pain had subsided to a great extent and the patient evidently felt quite better. A diagnosis of pyelitis was made by the physician; when urine examination was made, pus cells were found in the urine. The temperature kept going down and the abdominal pain kept subsiding, when suddenly the patient began to complain of severe earache and within thirty-six hours the drum had to be lanced, relieving a great amount of pus. Since then the patient has been kept in bed. She complains of pain soon after eating and still shows pus in the urine, while the temperature ranges between 99 by rectum in the morning and 101 in the evening. The ear still discharges. A second count was made twenty-four hours after the first one. It showed a differential of 78 per cent polymorphonuclears, with a total of 14,500 white cells. The patient feels apparently well, is playful, eats well and sleeps well. She is kept in bed, is given plenty of fluids, and in the beginning of her illness when the urine was markedly acid the alkaline method was used; at the present time she is getting a combination of methenamine and acid sodium phosphate. She was also given the dye treatment. The pus still persists. Is there any special method of treating the pyelitis? Is the autogenous vaccine treatment indicated? What is the maximum limit of liquid consumption in similar cases for a child 6 years old? Is there any special diet to follow? Kindly omit name.

M.D., Connecticut.

ANSWER.—The symptoms enumerated are certainly suggestive of acute appendicitis, and in spite of the pyuria the patient may indeed have had a subacute appendicitis that subsided spontaneously. The fact that she still complains of pain after eating may be significant, more so of a residual appendiceal or other intestinal disturbance than of the urinary tract.

Pyelitis may be present, but the writer does not state the amount of pyuria. The fever may, however, be due to the residual ear infection alone or to a combination of this and the subsiding appendicitis. Infection in two or three areas would suggest the possibility of a low grade septicemia.

Hematuria is occasionally a confusing complication of appendicitis, but it fortunately does not occur frequently. A degree of pyuria may also occasionally be seen with acute appendicitis, and both hematuria and pyuria have been explained on the basis of an extension of the inflammation from a retroplaced appendix to the right ureter. Some years ago, G. L. Hunner called attention to the fact that acute attacks of appendicitis may sometimes be accompanied by pus and blood in the urine when the clinical picture is one of septicemia, and also that acute pyelitis may result from acute appendicitis (acute Pyelitis Due to Acute Appendicitis, THE JOURNAL, April 25, 1908, p. 1328).

As long as the ear infection is present, a small amount of pyuria might be expected to persist. If the degree of pyuria is significant (more than 10 to 15 pus cells to a high power microscopic field), further support for the diagnosis of infection of the urinary tract is in order. A catheter specimen of the urine should be examined for red blood cells, albumin and casts, as well as for pus. A urine culture, a blood culture and an estimation of blood urea should be made. A pyelogram and cystoscopic examination may be necessary, perhaps also a roentgenogram of the mastoid area on the affected side.

Bed rest should be continued. Cathartics should be avoided entirely or used with caution. The diet should be confined to liquids and soft foods as long as fever and pain after meals are present. If the diagnosis of pyelitis is confirmed, and if the offending organisms are of the Escherichia type, the use of the ketogenic diet may be indicated. (See Queries and Minor Notes, THE JOURNAL, Oct. 28, 1933, p. 1413, and May 19, 1934, p. 1702.)

LIPOID NEPHROSIS

To the Editor:—Will you kindly inform me of a successful method of treatment for lipoid nephrosis that may have recently come to attention. A white boy, aged 5 years, in whom the onset occurred one and one-half years ago, was first hospitalized one year ago. The symptoms occurred at first only during intercurrent infections but became gradually more severe and persistent. He was treated with a high protein diet, urea hydrochloride and thyroid gland; he apparently improved. The edema and ascites disappeared but the urine continued to show large quantities of albumin and occasionally a few red blood cells. At home he did well until an acute infection of the upper respiratory tract brought a return of symptoms, more marked than ever. He has been in the hospital again for the past six months and the edema and ascites seem to resist any diuretic used but subside and increase more or less periodically independent of the medication. He has been relatively free from intercurrent infection during the past six months. The tonsils and infected teeth were removed during his previous stay. The red blood cells are increasing in numbers in the urine, probably indicating a complicating nephritis. Abdominal paracentesis has recently been required to relieve the ascites. The following diuretics were used: urea hydrochloride, ammonium nitrate, theobromine sodiosalicylate and salyrgan.

M.D., New York.

ANSWER.—True lipoid nephrosis is a relatively rare condition, especially in a child, and such a diagnosis demands certain definite criteria that distinguish lipoid from other types of nephrosis. There are three types of nephrosis: 1. Acute nephrosis: This type may arise from chemical poisons (e. g., mercuric chloride), from jaundice, or from certain toxic and infectious processes. It is characterized by oliguria and retention of urea and by little else. Anemia, hypertension, hypercholesterolemia and alterations in serum proteins are absent. Albuminuria may be only slight, and little if any edema and hematuria are noted. 2. Lipoid nephrosis: In lipoid nephrosis, hypertension, anemia and hematuria are absent but there is marked albuminuria and edema, a striking decrease in serum proteins and an increase in blood fats, especially in cholesterol, all in conjunction with good renal function. 3. Amyloid nephrosis: In this type of nephrosis, hypertension is also generally absent but there is marked albuminuria and edema, hypercholesterolemia and a decrease in serum proteins. Additional signs of renal insufficiency may be present; for example, a little hematuria, mild or moderate oliguria, and urea retention.

The treatment used so far in this case is quite in accord with the best practice. In addition to removal of foci of infection and to the use of the diet and diuretics mentioned, it is assumed that the patient's salt and water intake has been kept as low as possible, no extra salt being allowed, or the patient restricted to a salt-free diet and to not more than from 600 to 800 cc. of fluid daily. It would be well to have a roentgenogram and a special examination of the sinuses to rule out quiescent sinusitis, an infection sometimes missed in children and considered of more than ordinary importance in nephrotic children. The protein intake can be liberal, if renal function is adequate. As hematuria is present and is increasing, it is likely that the patient is suffering from a nephrotic type of nephritis and not from a true lipoid nephrosis; therefore an estimation of the blood urea (or if this is not feasible in a child, of the salivary urea index) would seem advisable before allowing excess protein to be given or before considering the further use of salyrgan, perhaps in combination with other diuretics.

The action of diuretics is characterized at times by variability; a diuretic may fail at one period of nephrosis and succeed at another. If the further use of ammonium nitrate by mouth and salyrgan intravenously in acceptably large doses is unsuccessful, the use of intravenous dextrose (about 100 cc. of a 15 to 20 per cent solution) or repeated small transfusions may be helpful. The purine (xanthine or caffeine) diuretics have apparently been used. Digitalis might be tried if there is any evidence of cardiac insufficiency.

Recently, Hartmann has advocated the use of acacia in cases of lipoid nephrosis not responding to other measures.

Diuretics in combinations may succeed, while they may fail when used individually. If considerable ascites is present, the child should not be permitted to lie too flat on the bed. Two or more pillows should be used, as "uremic convulsions," even in the absence of significant azotemia, have been noted in patients with nephrosis and extensive edema who were prone for long periods.

References:

Binger, M. W., and Keith, N. M.: The Effect of Diuretics in Different Types of Edema, THE JOURNAL, Dec. 23, 1933, p. 2009.

Hartmann, A. F.: Use of Acacia in the Treatment of Edema, abstr. THE JOURNAL, Jan. 7, 1933, p. 68.

TRYPARSAMIDE AND OPTIC ATROPHY

To the Editor:—A man, aged 66, had a marked arteriosclerosis and a blood pressure of 170 systolic, 100 diastolic. The Kahn test for syphilis was four plus. He had had rather intensive treatment. The drug that he had recently had weekly for a number of weeks was probably tryparsamide. The knee jerks were absent and the Romberg slightly positive; the pupils reacted sluggishly to light. The spinal fluid was normal. The most alarming symptom was that for the past two months the patient's vision had been progressively failing. Ophthalmoscopic examination showed a beginning optic atrophy. Is the tryparsamide responsible for the beginning atrophy in the optic nerve? What is the prognosis in this case? What are the indications for treatment? The man is now being treated merely with bismuth compounds and iodides, as I am afraid to give him either arsphenamine or tryparsamide. Please omit name.

M.D., Illinois.

ANSWER.—L. L. Mayer and R. Dentin Smith are of the opinion that tryparsamide causes no increase in atrophy of the optic disk when syphilis has previously caused changes, that tryparsamide causes no optic atrophy in unaffected disks, and that the drug under careful supervision should have only beneficial effects on the optic nerve. N. K. Lazar (Effect of Tryparsamide on the Eye, *Arch. Ophth.* **11**:240 [Feb.] 1934) concludes: "The definite loss of vision so soon after injection of tryparsamide leaves no doubt in my mind of a definite toxic effect of the drug in the visual apparatus of certain patients." Emory Hill in the discussion of this paper states there is no serious permanent damage to vision when the drug is stopped as soon as slight damage becomes apparent.

Cases of sudden blindness (twenty-four hours) have occurred following a single injection of a bismuth compound intramuscularly in cases of partial optic atrophy. Many authors have reported ill effects from the use of arsphenamine and neoarsphenamine in cases of partial optic atrophy. The question is unsettled. Satisfactory results have followed the use of the arsenicals unless the patients show decreasing peripheral fields or increasing pallor of the disks. Cases have been checked by the use of these drugs in the stage in which the patients first presented themselves. In cases showing untoward results from tryparsamide it is believed that the changes are due to the syphilis and not to the drug. With a negative serologic examination, most cases remain in the stages in which they are first seen. The indications for treatment are visual disturbances with normal fields, and treatment should be continued if the fields remain unchanged.

TREATMENT OF LATENT SYPHILIS

To the Editor:—The article in THE JOURNAL, April 21, page 1267, on the standard treatment procedure in early syphilis, will prove of great value to many physicians. I think that a similar summary of the treatment of late syphilis would be of great help to the general practitioner, who must treat many of these cases if they are to have any treatment. Kindly answer the following for me: Mrs. H., aged 34, came to me, Jan. 3, 1933, with a 4 plus Wassermann reaction. Her only complaint was that the tibial crests were sore and rough. During the first year I gave her twenty-six doses (most of them 0.6 Gm.) of neoarsphenamine, and forty-four 2 grain (0.13 Gm.) doses of bismuth salicylate in oil. At the end of the year the blood Wassermann reaction was 1 plus. Since April 1934 she has had ten doses of the bismuth compound and three doses of (0.45 Gm.) neoarsphenamine. Her veins are difficult to enter with a needle. Is there an efficient method of treatment that does not necessitate the frequent use of intravenous injections or does not use them at all. I would appreciate any sugestions regarding this case.

M.D., Kansas.

ANSWER.—The inquirer will find in at least three textbooks recently published adequate information in regard to the general principles of the treatment of late syphilis. The degree of individualization is such that it is difficult to summarize without excessive detail. The Cooperative Clinical Group has, however, published accounts of the treatment of latent syphilis, which are available through the United States Public Health Service, Bureau of Venereal Diseases.

The patient described stands at the moment more in need of adequate examination than in need of further treatment. It is essential to determine the status of the nervous system by a complete spinal fluid examination, and of the cardiovascular mechanism by a careful physical examination, a teleroentgenogram, fluoroscopic visualization of the aorta and an electrocardiographic examination. The blood Wassermann reaction is, in some respects, the least important item in the case. The patient has received at least the average amount of treatment appropriate to a latent infection. If the soreness of the tibial crests was due to a periosteal or osteoperiosteal lesion, she must be regarded as having late bone syphilis and the heavy metal therapy should be continued for approximately another year. If her treatment is to be confined to intramuscular procedures, bismuth arsphenamine sulphonate once a week for forty injections, or a continuance of bismuth salicylate in courses of ten injections separated by intervals of from eight to twelve weeks during which the patient receives potassium iodide would be an average appropriate procedure in the absence of contraindications or evidence of more serious forms of involvement.

The fact that the patient is a woman must be kept in mind with particular reference to pregnancy, and if she becomes pregnant treatment with neoarsphenamine and a bismuth compound should be resumed for the protection of the child, in accordance with the principles applicable to this aspect of syphilis.

INTERMENSTRUAL PAIN AND OVULATION

To the Editor:—A woman, aged 25, married, never pregnant, complains of acute pain, which has recurred regularly every month, midway between her menses, for the four years of her married life. It is localized in the lower right abdominal quadrant. It is sudden in onset, endures for two or three hours and ceases as suddenly as it begins. A soreness remains at the site for two days. For two days preceding and following the pain she regularly notes an opaque leukorrhea, which occasionally shows flecks of blood. It is never present at other times. The patient has never been seriously ill; no history of pelvic inflammatory disease was obtained. Her menses began at 15 and were rather profuse, recurring at slightly irregular intervals, associated with cramps and occasional vomiting. The intermenstrual pain is not associated with vomiting. Examination of the external genitalia is negative. The uterus is of normal size, anteflexed and moderately retroverted, and is not fixed. There are no palpable masses or palpable abnormalities of the tubes or ovaries. The examination is attended by considerable tenderness on the right side of the pelvis. The patient is apprehensive of the pain and states that she would be perfectly well were it not for that. She is completely disabled at the time. No abnormalities have been found in the urine or blood. There is no fever. Will you kindly suggest the probable diagnosis and treatment in this case? Please omit name and address.

M.D., Iowa.

ANSWER.—The pain described is that which is termed "mittelschmerz" by the Germans and was called intermenstrual pain by Priestley. It recurs regularly at the same time in the intermenstrual cycle, but usually about midway between each two menstrual periods. The condition is not common and a diagnosis of intermenstrual pain should not be made unless the pain recurs at about the same time for at least a number of months. During periods of amenorrhea such as pregnancy and lactation, the attacks of pain are absent. The pain, which is not characteristic, is usually confined to one iliac fossa but sometimes to both. It usually lasts a few hours but may endure for days, although in the latter cases it is not steady. In about 50 per cent of the cases of intermenstrual pain there is a vaginal discharge present during the attacks of pain. The discharge may be watery, mucous, yellowish and occasionally bloody. In some cases in which the discharge is bloody or blood stained there is a local cause for the bleeding, such as a polyp or submucous fibroid. However, as C. G. Hartman (*Am. J. Obst. & Gynec.* **19**:511 (April) 1930) points out, the bleeding associated with intermenstrual pain may be a pathologically accentuated expression of a phenomenon that occurs in some animals. Many individuals regard as menstruation the visible periodic bleeding of bitches. This designation is wrong, as evidenced by its time relation to ovulation. The bleeding precedes and accompanies ovulation and hence should be called "proestrous bleeding." A similar and homologous bleeding occurs at the cotyledons of the cow. The final proof of the homology is Hartman's discovery of the intermenstrual bleeding in the monkey, which frequently occurs in the middle of the menstrual cycle. It is usually microscopic, is always less than in the dog, and is in both species a concomitant of the congestion that accompanies the presence of a maturing follicle. Hartman wonders whether future study will not show that intermenstrual bleeding in the human female is physiologic and normal rather than abnormal.

Most of the women afflicted with intermenstrual pain are young, but the attacks of pain rarely make their appearance with the onset of puberty. The attacks may recur for many

years, even lasting throughout the entire reproductive period. A large proportion of these women are sterile. The menstrual periods are usually normal and, if dysmenorrhea is present, it is usually much less severe than the intermenstrual pain. Many, but by no means all of the women who suffer intermenstrual pain have pelvic disease.

The cause of the pain is undoubtedly the process of ovulation, which occurs at about the middle of the intermenstrual interval. Hence the pain is associated with the menstrual period that follows the pain and not the one which precedes it. It is difficult to say what factors are involved in the mechanism of production of the pain. Normal ovulation is not associated with pain.

The treatment of intermenstrual pain is unsatisfactory. In not one of the sixty-four instances collected from the literature by Kelly was the pain self limited (Kelly H. F.: Medical Gynecology, New York, D. Appleton & Co., 1908). Of course, if any abnormality in the pelvis is present, it should be corrected by medical, physical or surgical means. The pain itself must be treated empirically by means of rest in bed, local heat and mild analgesic drugs. In many instances, narcotics such as codeine and morphine must be given; but they must be used with great caution. Kelly states that removal of the ovary on the side where the attacks of pain always occurred brought about relief in only two out of four cases. Whether any of the new hormone preparations will bring about a cure is highly conjectural.

PROGRESSIVE FATIGUE AND HYPERTENSION

To the Editor:—A white man, aged 45, states that for three years he has been becoming more and more constantly tired. Aside from this his history is negative. Physical examination is negative except for a slight hyperactivity of the knee jerks and a blood pressure of 148 systolic, 110 diastolic. Urinalysis is negative except for a few epithelial cells and a few white cells. Hemoglobin is 85; the red cells number 4,800,000 and the white cells 7,800. The basal metabolic rate was —4 and —2.5 on two tests. The Wassermann reaction is negative. A trial of thyroid therapy gave no results. Please omit name. M.D., Illinois.

ANSWER.—The two positive observations in this case are progressive fatigue and early essential hypertension. As a rule, subjects in the early stage of essential hypertension do not become fatigued easily. Many are extremely resistant to abnormal degrees of mental and physical fatigue. States of exhaustion are more prone to occur among patients who have low blood pressure. It is likely that there is no endogenous element underlying the patient's complaint. It is more probable that exogenous factors, such as work, worry and mental stress and some constitutional inadequacy rather than any derangement in the body, are causing the state of fatigue. If low metabolic rates or advanced grades of focal infection are absent, and if organic disease is eliminated, the condition of patients may improve when assured that their physical functions and organs are not diseased, as this removes a factor of anxiety which accentuates fatigue. Adequate vacations, with changes in environment, more sleep, midday rest and week end periods of relaxation, combined with mild forms of physical exercise, bring about a feeling of well being. If this treatment does not prove efficacious, glycine might be given a trial for a period of two or three months. Reduction in the amount of tobacco used or elimination of other deleterious habits may be advised, although too drastic changes in habits should not be urged.

CALCIUM DEPOSITS IN BRONCHIAL TUBES

To the Editor:—I have a patient who has calcium formations in the bronchial tubes. For fifteen years she has coughed up calcium stones at intervals. The condition has been diagnosed as broncholithiasis. The suggested treatment was rest, tonics and codeine for the cough. The patient does not improve with this treatment and I am asking you for further information on the care and treatment of the disease. The climate here is damp and cold. Would a dry warm climate be beneficial to the patient? Please omit name and town. M.D., Missouri.

ANSWER.—Abnormal deposits of calcium occur in the tissues of the chest under much the same conditions as in other portions of the body. Abnormal calcification occurs at the site of hyalinized tissue in regions of old suppuration or hemorrhage and also in cases in which there is excessive mobilization of calcium in diseases of the bones. Metastases in malignant disease may become calcified. In the chest, extensive calcification of the pleura has followed empyema. A frequent site of localized calcification and perhaps that most frequently associated with expectoration of calculi is the glands at the hili of the lungs. Smaller calcified nodules are commonly seen in roentgenograms of the lung fields. Many of the lesions are associated with tuberculosis, but in a considerable number of the cases cited in the literature no tuberculosis was demonstrable and after expectoration of calcareous masses the patients recovered and remained clinically well for years. In other instances a period of good health was followed by recurrence of the expectoration of calculi.

A calcareous mass may cause erosion of an adjacent bronchus, with subsequent expectoration of calcified fragments. These fragments may vary in diameter from 1 mm. to 1 cm. and are sometimes larger. Their composition is usually that found in calcium deposits elsewhere, approximately 85 per cent calcium phosphate and 15 per cent calcium carbonate. The expectorated masses have been called broncholiths, bronchial calculi and lung stones. In some instances a calculus becomes fixed in a bronchus, causing retention of secretions, formation of an abscess or local pulmonary inflammation.

In the case cited, some information as to the possible nature of the underlying process should be supplied by roentgenograms of the chest, which would perhaps reveal evidence of an old calcified pleura or of lesions at the hilus. Four cases have been reported by J. J. Lloyd (Broncholiths, *Am. J. M. Sc.* **179**:694 [May] 1930), in one of which a calcified mass at the right hilus, demonstrated by a roentgenogram, was shown to have disappeared in later films taken after the expectoration of broncholiths.

The further course of the condition described in the query will depend to a considerable extent on the presence or absence of active clinical tuberculosis. The bronchoscope might be of value in diagnosis and possibly, as suggested by Chevalier Jackson, in treatment. A warm dry climate would be likely to favor recovery in the presence of an associated tuberculosis or in nontuberculous chronic bronchitis.

Among other references the following two articles may be consulted:

Wells, H. G.: Calcification and Ossification, *Arch. Int. Med.* **7**:721 (June 15) 1911.

Pritchard, J. S.: Calcareous Degeneration Found in the Thorax, *Arch. Int. Med.* **32**:259 (Aug.) 1923.

TREATMENT OF STERILITY

To the Editor:—Can you give me suggestions regarding a case of sterility? A man, aged 24, has been married four years. As a boy, he had mumps with orchitis; there is no history of venereal infection. Condom specimens of semen show many inactive spermatozoa. The prolonged administration of emplets of orchic substance (Parke, Davis & Co.) produces improvement, but this is not maintained. The wife, aged 23, has fairly regular but scanty menstrual periods. The uterus is rather of the infantile type. There is no erosion of the cervix and no definite cervicitis. Postcoital semen removed from cervix shows a hostile reaction of the cervical secretions to the spermatozoa, no active spermatozoa being found. The cervix has been dilated. Small doses (0.1 cc.) of anterior pituitary-like principle from pregnancy urine have been given three times a week for two weeks during each intermenstrual period. Semen has been introduced into the uterine cavity through a cannula without results. I should appreciate any help you can give me. Kindly omit name. M.D., Georgia.

ANSWER.—Condom specimens are generally unsatisfactory. It is far better to have the husband ejaculate the semen into a small, clean, wide-mouthed jar or bottle at the time of the orgasm. A friction specimen is more satisfactory than a condom specimen. If no motile spermatozoa are seen after repeated examinations of specimens in containers and the semen obtained from the vagina and cervix after coitus, the husband should be investigated by a urologist to see whether the condition can be rectified. Underdevelopment of the uterus is frequently a cause of sterility.

In spite of the excellent results observed in animal experiments with the use of injections and implantations of pituitary substances, the results in human beings have not been highly satisfactory. However, the outlook for this type of therapy is encouraging.

No mention is made of a tubal patency test. This test should be performed before semen is injected into the uterine cavity because, if the uterine tubes are not permeable, not only will pregnancy fail to take place but infection may result. The tubal patency test should not be done unless it is demonstrated that the spermatozoa in the husband's semen are satisfactory.

If the spermatozoa are satisfactory and the tubes are patent, it may be advisable to perform a dilation and curettement on empirical grounds. Not infrequently, pregnancy follows this operation.

Semen should not be injected into the uterine cavity unless a large proportion of the spermatozoa are actively motile. Furthermore, in most instances the semen must be injected many times before fertilization takes place. The most favorable time for uterine insemination is during the middle ten days between menstrual periods, because ovulation occurs during these ten days in the vast majority of women.

EDEMA OF ANKLE DURING MENSTRUATION

To the Editor:—A woman, aged 28, had a miscarriage, Sept. 1, 1933. Since that time she has had severe pain in the right ankle. The pain starts one day before the menstrual period and lasts for about six days. The pain is severe enough to cause the patient to limp and is continuous, whether she is on her feet or resting. There is also swelling between the achilles tendon and the external and internal malleolus. There are no varicose veins present and the leg is apparently normal, the only swelling being between the achilles tendon and the malleolus. Between periods she has occasional twitching in this region. The pain and swelling have continued with each menstrual period since the miscarriage. The swelling is not of the edematous type. I have treated her for some time but have not been able to obtain any results. Will you kindly tell me the cause of this condition, and also the proper treatment? Please do not mention my name.

M.D., Michigan.

ANSWER.—Assuming that the patient had an uneventful recovery from her miscarriage, it is difficult to see any connection between the miscarriage and the present complaint. Likewise there is no apparent direct relationship between the menstrual periods and the pain and edema in the ankle. As is well known, menstruation does not simply consist of uterine bleeding but affects all parts of the body. This results in a number of other signs and symptoms, many of which are disagreeable and troublesome. Among them are pains in the pelvis, pain in the breasts, headaches, circulatory disturbances, lassitude, nervousness, bladder irritability, interference with the regularity of the bowel movements, overactivity of the skin, and skin eruptions. In other words, the process of menstruation involves the entire body and if for some reason the right ankle is a locus minoris resistentiae, it may present the features this patient experiences when a change takes place in the body each month. The edema and the pain are most likely of circulatory origin. Since the exact cause of the pain is unknown, no specific therapy can be recommended. The patient should be made as comfortable as possible by physical measures and mild analgesic drugs. Even though there is an association with the menses, the use of hormone preparations would be highly speculative. Most likely the symptoms will disappear spontaneously just as usually happens when similar disturbances arise in connection with the menstrual periods.

IDENTIFICATION OF SEMINAL STAINS

To the Editor:—A man was found unconscious with bullet wounds in the upper right part of the chest, the upper right part of the abdomen (the bullet coursing backward and downward toward the sacral region), and another through the scrotum. The undertaker, on examining the victim's clothes found, as he thought, stains due to a seminal discharge. The prosecuting attorney contends that this emission was due to the bullet wounds, in contradiction to testimony for the defense that the victim was having illicit relations with the murderer's wife just prior to the shooting, in spite of the fact that the victim's clothes were all buttoned up and evidence points toward his becoming unconscious immediately on being shot. The question is, Is it possible to be shot in the region of the pelvis or scrotum with resulting seminal discharge? Kindly omit name.

M.D., Kentucky.

ANSWER.—That emission of semen by ejaculation can follow a gunshot wound of the pelvis seems unlikely. On the other hand, semen might run out through a bullet wound involving the seminal vesicles. Let it be noted that the seminal nature of a stain cannot be determined by inspection only—spermatozoa must be demonstrated microscopically and/or seminal protein demonstrated by a specific precipitin test before one can say that a given stain is due to semen. Finally, in the case in question, assuming that the stains are seminal, why might they not have been deposited some time before the episode that led to the fatal shooting?

MERCURY POISONING HAZARD

To the Editor:—Will you please give me your opinion as to whether a laboratory worker who is handling mercury continuously, about six hours a day, five days a week, would be subject to mercurial poisoning? The mercury is used in liquid form from a buret in testing the tensile strength of paper. The room is well ventilated and he does not touch much of the mercury with his hands. Kindly omit name if this appeears in THE JOURNAL.

M.D., Wisconsin.

ANSWER.—Mercury poisoning from the exposure described is possible. Traces of mercury vapors continually arise from the surface of the metallic mercury. Novy, years ago, established the fact that the mercury in manometers used in connection with the culturing of various organisms gave off sufficient vapors to alter or inhibit the growth of these fungi or bacteria. The presence of mercury poisoning in this paper tester would be favored by the presence of one or more of the following cardinal manifestations: salivation, gingivitis, dryness of the throat, blue discoloration of the gums, muscular tremors and erethismus. Mercury in the atmosphere may be demonstrated through the use of mercury test papers, which may be applied in a manner as simple as that in which litmus paper is used for the determination of acids and alkalis. A good description of mercury poisoning may be found in a publication by Wade Wright (*J. Indust. Hyg.* **4**:296 [Nov.] 1922).

PELVIC MEASUREMENTS

To the Editor:—Please give me the average or normal pelvic measurements, especially the intercristal, interspinous, intertrochanteric, and external and internal conjugate. With what measurements do you consider cesarean section advisable? Please omit name and address.

M.D., California.

ANSWER.—The average external pelvic measurements are: interspinous, 26 cm.; intercristal, 29 cm.; intertrochanteric, 31 cm.; external conjugate, 20.5 cm.; internal conjugate, 11 cm.; diagonal conjugate, from 12.5 to 13 cm.

Of these measurements the internal conjugate and diagonal conjugate are the only ones of real value, but even they may not be used alone in deciding the necessity for cesarean section. The internal examination and the roentgenographic evidence are necessary in making up one's mind to perform such an important operation.

Repeated emphasis must be put on the fallacy of the external pelvic measurements.

The size of the baby must also be considered and finally, except in extreme contraction, a sufficient test of labor should be given.

DIGESTION OF MEAT

To the Editor:—Kindly inform me through THE JOURNAL about the duration of digestion of meat, such as steak, in the stomach and in the small intestine, and the total time interval between ingestion and absorption. Please omit name.

M.D., Chicago.

ANSWER.—Observations on these phenomena are so fragmentary as to the materials ingested, the species of animal used and the methods of observation as to render it almost impossible to give a forthright answer to these questions. Several authorities have been consulted, both personally and through their writings, with the following results, which must be evaluated in the light of the foregoing:

Meat leaves the stomach in from one to two and one-half hours. It continues to undergo digestion in the small intestine for about three hours, depending on the amount ingested. By the end of this time it is leaving the ileum, beyond which little absorption occurs. The total time between ingestion and the absorption of meat therefore ranges from four to six hours.

BRUISES OF SHIN

To the Editor:—I have a patient who bruised her shin fourteen years ago. At times an ulcer forms over the tibia at the site of the injury. This is extremely painful. Hot, wet dressings and staying off the feet will allow it to heal. Is there anything that can be used on it? What is the best treatment for these bruises over the shin bone when they occur?

DEVERE RITCHIE, M.D., Harrisburg, Pa.

ANSWER.—The circulation of the skin of the lower half of the leg over the tibia is poor, and following any injury slow healing often results.

Avoidance of infection and phlebitis favors early healing. Varicose veins increase the tendency to ulceration.

With any wound or ulcer of the leg, supporting bandages and keeping off the feet for a few days are of great help in healing.

Narrow strips of adhesive plaster applied across the chronic ulcer promote epithelization underneath. They are changed about twice a week and covered with a little gauze to absorb any secretion.

If varicose veins are present, they may be treated by injection or excision if necessary.

Skin grafts after excision of the ulcer and the fibrous tissue are indicated when other measures fail. A Wassermann test should always be done.

APHTHAE RESISTENTIA

To the Editor:—Could you advise me of some new methods to try in treating a case of chronic aphthae, or periadenitis mucosa necrotica recurrens? The case I am treating is that of a woman about 25 years old. She has had the condition off and on for about fifteen years. At times the lesions are numerous and severe and occasionally involve the vagina. She states that one of her children, a brother, her father and a grandmother are all afflicted with this disease. She gives a definite history of rheumatic fever and St. Vitus dance. Please omit name and address.

M.D., New York.

ANSWER.—As implied in the names, periadenitis mucosa necrotica recurrens, or aphthae resistentia, is a difficult disease to treat, clearing at times with or without treatment but nearly

always recurring. All authorities agree that it yields to arsenic more regularly than to any other drug. Ormsby has reported cases that cleared up with treatment with arsphenamine, but this drug failed in other cases. Howard Fox mentioned prompt improvement with roentgen therapy. Sutton, who originally described the disease in this country, used hygienic measures, outdoor sleeping, light exercise, easily digested, nourishing food in plenty, cod liver oil, iron and arsenic with good effect; the latter drug is possibly responsible for most of the benefit. The disease is familial, as in the case under discussion, seems to have a nervous element in it, and the mild lesions resemble ordinary canker sores. Whether it has any relation to the latter disease, or whether the resemblance to tuberculids mentioned by Fordyce in his discussion of Howard Fox's case means anything, has not been determined.

TUMOR OF THE KNEE JOINT

To the Editor:—A boy, aged 5 years, was brought to me because of a fluctuating tumor, about the size of a small hen's egg, in the left popliteal space. Aspiration showed a clear, viscid fluid. It was treated by incision and drainage and swabbing out of the cavity with a strong tincture of iodine, and drainage. The wound closed without infection in about ten days and the cavity seemed to have been obliterated. Now after a period of three months the tumor has reappeared and is gradually increasing in size. Advice is requested as to the probable nature of the tumor and whether excision is indicated. Please omit name and address.

M.D., California.

ANSWER.—It may concern an outpouching or hernia of the knee joint itself or an inflammation in some bursa in this region. After puncture, rest and fixation may result in cure. It must be borne in mind that a cyst in the popliteal region often opens into the knee joint. In some of the cases, tuberculosis is at the bottom.

THYMIC DEATH

To the Editor:—Concerning the query on "Thymic Death" in THE JOURNAL, September 15, page 856, much confusion on this subject has arisen because of classifying any unexplained death in children as "thymic." Thus, if the "lungs were completely atelectatic," the diagnosis in the case in question is suggestive of massive atelectasis due to aspirated mucus rather than of "thymic death."

In consideration of the causes of "thymic death," such theories as death due to mechanical pressure on the trachea and blood vessels, hemorrhages into the pons and asphyxiation due to contracting uterine walls should be mentioned only from a historical point of view, as they are no longer accepted.

There is increasing evidence that the enlarged thymus, like all lymphoid tissues, is a part of the allergic constitution and that sudden death is due to allergic shock (Waldbott, G. L.: So-Called Thymic Death, *Am. J. Dis. Child.* **47**: 41 [Jan.] 1934). This theory also conforms well with the familial occurrence of "thymic death." I have the records of four families in which "thymic death" occurred in more than one child.

Concerning roentgen treatment of the thymus, it is well to remember that death may occur in thoroughly irradiated babies, as my records show. This, however, does not speak against the fact that roentgen therapy of the gland is still the best method available.

GEORGE L. WALDBOTT, M.D., Detroit.

DEFORMITY OF RECTUM WITH PAIN AFTER REPEATED INFECTION

To the Editor:—I was much interested in your answer to M.D., Texas, in Queries and Minor Notes (THE JOURNAL, September 1, p. 699) concerning inflammation of the anal canal. Although I agree that the disease in question can hardly be called a neuralgia, I do not believe that the trouble is due to a deformity of the rectum. The history, symptoms and proctoscopic observations in this case are, in my opinion, very suggestive of gonococcic infection of the anal ducts. The latter are preformed structures of varying length which extend from the crypts of Morgagni into the wall of the anal canal. Their microscopic changes and clinical significance were described by Tucker and Hellwig in *Surgery, Gynecology and Obstetrics* (**58**: 145 [Feb.] 1934). I agree with you that the condition will not be cured by conservative treatment. In my cases of chronic gonococcic infection of the anal ducts I have obtained lasting cures only after complete excision of the infected ducts.

CLAUDE C. TUCKER, M.D., Wichita, Kan.

IMMUNITY IN TULAREMIA AND UNDULANT FEVER

To the Editor:—In answer to the query by Stanley M. Gates (THE JOURNAL, September 15, p. 861) you stated that tularemia and undulant fever appear to be good examples of diseases that develop final immunity with each succeeding exacerbation. In reference to tularemia, there are no authenticated reported cases of reinfection. Occasionally an individual who has had the disease may again manifest some of the lesser phases of the infection, which may be regarded as reinfection, recurrence or second attack. These manifestations of tularemia are rare. Francis makes the statement that he has not heard of a frank out-and-out second attack of tularemia. The immunity in tularemia is regarded to be the most complete of any of the infectious diseases.

HARRY L. BAER, M.D., Pittsburgh.

Council on Medical Education and Hospitals

COMING EXAMINATIONS

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Oral (Group A and Group B candidates).* San Antonio, Texas, Nov. 13-16. Sec., Dr. C. Guy Lane, 416 Marlborough St., Boston.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written (Group B candidates).* The examination will be held in various cities of the United States and Canada, Nov. 3. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: San Antonio, Texas, Nov. 12; Philadelphia, June 10. Sec., Dr. William H. Wilder, 122 S. Michigan Blvd., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: San Antonio, Texas, Nov. 13. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

ARKANSAS: *Basic Science.* Little Rock, Nov. 5. Sec., Mr. Louis E. Gebauer, 701 Main St., Little Rock. *Regular.* Little Rock, Nov. 12. Sec., Dr. A. S. Buchanan, Prescott. *Eclectic.* Little Rock, Nov. 13. Sec., Dr. L. L. Marshall, 820 W. 14th St., Little Rock. *Homeopathic.* Fayetteville, Nov. 13. Sec., Dr. Allison A. Pringle, Eureka Springs.

CONNECTICUT: *Regular.* Hartford, Nov. 13-14. *Endorsement.* Hartford, Nov. 27. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Homeopathic.* New Haven, Nov. 13. Sec., Dr. Edwin C. M. Hall, 82 Grand Ave., New Haven.

FLORIDA: Tampa, Nov. 12-13. Sec., Dr. William M. Rowlett, Box 786, Tampa.

KENTUCKY: Louisville, Dec. 4-6. Sec., State Board of Health, Dr. A. T. McCormack, 532 W. Main St., Louisville.

MAINE: Portland, Nov. 13-14. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton Jr., 192 State St., Portland.

MASSACHUSETTS: Boston, Nov. 13-15. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 144 State House, Boston.

MISSOURI: Kansas City, Oct. 24. State Health Commissioner, Dr. E. T. McGaugh, State Capitol Bldg., Jefferson City.

NEBRASKA: Lincoln, Nov. 22-23. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: Carson City, Nov. 5. Sec., Dr. Edward E. Hamer, Carson City.

NORTH CAROLINA: *Endorsement.* Raleigh, Dec. 3. Sec., Dr. Benj. J. Lawrence, 503 Professional Bldg., Raleigh.

OHIO: Columbus, Dec. 3-6. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OREGON: *Basic Science.* Portland, Nov. 17. Sec., Mr. Charles D. Byrne, University of Oregon, Eugene.

SOUTH CAROLINA: Columbia, Nov. 13. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

TEXAS: Galveston, Nov. 20-22. Sec., Dr. T. J. Crowe, 918 Mercantile Bank Bldg., Dallas.

WEST VIRGINIA: Martinsburg, Oct. 29-31. State Health Commissioner, Dr. Arthur E. McClue, Charleston.

Maryland June Examination

Dr. Henry M. Fitzhugh, secretary, Board of Medical Examiners, reports the written examination held in Baltimore, June 19-22, 1934. The examination covered 9 subjects and included 90 questions. An average of 75 per cent was required to pass. One hundred and sixty-three candidates were examined, 154 of whom passed and 9 failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists	(1933) 82.1, (1934) 86.7, 87.4, (1934) 81.1		87.5
George Washington University School of Medicine	(1933) 83.3, (1933) 77.1, 78, 81.7, 83.5, 84.3, 85.7, (1934) 78.2, 79.1, 79.2, 79.4, 80.4, 80.4, 81.3, 82, 82.2, 83, 83.3, 83.5, 83.6, 85, 85.7, 85.8, 86.2, 88.2, 90.3, 90.4		86.4,
Georgetown University School of Medicine	(1932) 81.2, (1932) 86.4, 88.5, (1934) 76.7, 78.3, 79.4, 79.7, 79.7, 80.3, 81.3, 82.1, 82.2, 82.6, 84.1, 84.3, 85.2, 85.6, 86, 86.2, 86.2, 86.7, 86.8, 86.8, 87.5, 87.5, 87.6, 88.2, 88.3, 88.3, 89, 89.4, 89.7, 89.8, 89.8, 90.1, 91.6, 92.5		81.1,
Howard University College of Medicine	(1933) 77, 80.2, 81.5, 83.5, 83.8		
Tulane University of Louisiana School of Medicine	(1933)		81.5
Johns Hopkins University School of Medicine	(1931) 87.5, (1934) 80, 80; 81, 81.5, 81.6, 81.6, 82.1, 82.3, 82.7, 82.8, 83.3, 83.6, 84, 84.3, 84.5, 84.6, 84.8, 84.8, 84.8, 85.1, 85.2, 85.4, 85.4, 85.4, 86, 86.3, 86.3, 86.4, 87, 87.3, 87.4, 87.4, 87.5, 87.6, 87.6, 87.7, 87.8, 88.2, 88.3, 88.4, 88.5, 88.7, 89, 89.3, 89.3, 89.3, 89.4, 89.4, 89.7, 89.8, 90.2, 90.4, 90.5, 90.5, 91, 91, 91.1, 91.6, 92.4, 93		80.4,
Univ. of Md. School of Med. and College of P. and S.	(1932) 83.3, (1932) 86.4, 88.5, (1934) 76.7, 78.3, 79.4, 79.7, 79.7, 80.3, 81.3, 82.1, 82.2, 82.6, 84.1, 84.3, 85.2, 85.6, 86, 86.2, 86.2, 86.7, 86.8, 86.8, 87.5, 87.5, 87.6, 88.2, 88.3, 88.3, 89, 89.4, 89.7, 89.8, 89.8, 90.1, 91.6, 92.5		88.1,
University of Michigan Medical School	(1931)		88
University of Nebraska College of Medicine	(1933)		89.6
Albany Medical College	(1932)		83.1
Jefferson Medical College of Philadelphia	(1934)		89.5
University of Pennsylvania School of Medicine	(1931)		82.8
University of Pittsburgh School of Medicine	(1933)		82.4
University of Tennessee College of Medicine	(1930)		78.1
University of Virginia Department of Medicine	(1931)		87.3
McGill University Faculty of Medicine	(1928) (1929) 86.2, (1930) 79		82.2,
Univ. de la Habana Facultad de Medicina y Farmacia	(1926)		80.4
Licentiate of the Royal College of Physicians of London and Member of the Royal Coll. of Surgs. of England	(1934)*		84.6
Université de Genève Faculté de Médecine	(1934)*		79.6

School	FAILED	Year Grad.	Per Cent
Georgetown University School of Medicine		(1934)	72.4, 73.2, 74.7, 75.5,† 76.5,‡ 77.5 †
Regia Università degli Studi di Roma Facoltà di Medicina e Chirurgia		(1932)	64.4
Regia Università di Napoli Facoltà di Medicina e Chirurgia		(1923) 51.2, (1931)*	63.4

One physician was licensed at a special examination held June 5. The following school was represented:

School	PASSED	Year Grad.
University of Manitoba Faculty of Medicine		(1921)

Eighteen physicians were licensed by reciprocity and 7 physicians were licensed by endorsement from March 2 to August 2. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
George Washington University School of Medicine		(1905)	Dist. Colum.
Georgetown University School of Medicine		(1929)	New Jersey
Rush Medical College		(1914) D. C., (1929)	Illinois
Indiana University School of Medicine		(1931)	Indiana
Tulane University of Louisiana School of Medicine		(1932)	Louisiana
Long Island College Hospital		(1928)	New York
University of Buffalo School of Medicine		(1901)	New York
Eclectic Medical College, Ohio		(1927)	Ohio
Western Reserve University School of Medicine		(1926)	Ohio
Jefferson Medical College of Philadelphia		(1931)	N. Carolina, (1932) Pennsylvania
Meharry Medical College		(1930)	Tennessee
University of Texas School of Medicine		(1928)	Texas
Medical College of Virginia		(1930)	Virginia
Univ. of Va. Dept. of Med		(1931), (1932), (1933)	Virginia

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists		(1934)	N. B. M. Ex.
Johns Hopkins University School of Med.		(1929, 2), (1931)	N. B. M. Ex.
Harvard University Medical School		(1928)	N. B. M. Ex.
Woman's Medical College of Pennsylvania		(1933)	N. B. M. Ex.
University of Toronto Faculty of Medicine		(1927)	N. B. M. Ex.

* Verification of graduation in process.
† Deficient in one subject.
‡ Deficient in three subjects.

Maine July Report

Dr. Adam P. Leighton Jr., secretary, Board of Registration of Medicine, reports the written examination held in Augusta, July 5-6, 1934. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Twelve candidates were examined, all of whom passed. Five physicians were licensed by reciprocity and 3 physicians were licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Georgetown University School of Medicine		(1933) 82, (1934)	84
Boston University School of Medicine		(1932) 85, (1933)	86
Harvard University Medical School		(1932)	86
Tufts College Medical School		(1931)	79
Long Island College of Medicine		(1933)	87
Jefferson Medical College of Philadelphia		(1934)	78, 79
University of Toronto Faculty of Medicine		(1892) 77, (1931)	81
McGill University Faculty of Medicine		(1928)	86

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
George Washington University School of Medicine		(1931)	Maryland
Georgetown University School of Medicine		(1932)	Maryland
Johns Hopkins Univ. School of Med.		(1926), (1928)	Maryland
Washington University School of Medicine		(1931)	Missouri

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Yale University School of Medicine		(1932)	N. B. M. Ex.
Harvard University Medical School		(1929), (1932)	N. B. M. Ex.

Mississippi June Report

Dr. Felix J. Underwood, secretary, Mississippi State Board of Health, reports the written examination held in Jackson, June 26-27, 1934. The examination covered 12 subjects and included 96 questions. An average of 75 per cent was required to pass. Twenty-nine candidates were examined, 28 of whom passed and 1 failed. Thirteen physicians were licensed by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Emory University School of Medicine		(1932) (1934)	89.5, 79.9, 80.7, 81.2, 82.3, 83.5, 83.6, 84.1, 87.7, 87.8
Rush Medical College		(1934)	84.3*
University of Louisville School of Medicine		(1934)	85.4
Louisiana State University Medical Center		(1934)	82.4*
Tulane University of Louisiana School of Medicine		(1934)	79.5, 83.8, 84.1, 85, 85.6, 87.4, 87.9
University of Pennsylvania School of Medicine		(1934)	85.5
University of Tennessee College of Medicine		(1932) 89.8, (1934)	83.2
Vanderbilt University School of Medicine		(1931) (1934) 87.9, 88.5, 88.8	83.5,
Nongraduate †			77.7

	FAILED	Per Cent
Nongraduate †		41.2

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Emory University School of Medicine		(1929)	Georgia
Northwestern University Medical School		(1931)	Alabama
Rush Medical College		(1885)	Wisconsin
School of Med. of the Div. of the Biological Sciences		(1933)	Oklahoma
Tulane Univ. of La. School of Med.		(1925), (1929), (1932)	Louisiana
Meharry Medical College		(1932)	Tennessee
University of Tennessee College of Medicine		(1929), (1931), (1932), (1933)	Tennessee
Vanderbilt University School of Medicine		(1924)	Louisiana

* This applicant has completed his medical course and will receive an M.D. degree and Mississippi license on completion of internship.
† Permitted to come before the board for examination by special act of legislature.

Book Notices

Parasitism and Disease. By Theobald Smith. Published on the Louis Clark Vanuxem Foundation. Cloth. Price, $2. Pp. 196. Princeton: Princeton University Press, 1934.

The director emeritus of the department of animal pathology of the Rockefeller Institute of Medical Research is abundantly qualified by long contact with research on parasitism and disease to make a critical presentation of this subject in the light of his long and varied experiences with the experimental analysis of the factors in disease and its prevention and control. His discovery of the relation of the cattle tick to the Texas fever of cattle opened the relation of insect vectors to the transmission of disease of parasitic origin, a relation that was basic to the later analysis and solution of the causes of malaria, trypanosomiasis, leishmaniasis, typhus fever and other insect-borne afflictions of man and the domestic animals.

The lectures here expanded and modified in book form were delivered on the Louis Clark Vanuxem Foundation. The book lacks the illustrations that accompanied the lectures but retains the freedom from citation of authorities and documentation of sources which the platform demands. Both of these features tend to disappoint the technical reader, though this is in part assuaged by the greater simplicity of presentation and a certain directness in criticisms and the statement of conclusions.

The author's recognition that animal and human parasitic afflictions present a common series of problems for analysis requiring similar, if not identical, methods of attack, with solutions equally applicable in therapy, prevention and control alike in veterinary and human medicine, presents a point of view much needed in these days of subsidized organizations of antivivisectionists. A continuous campaign of education of the public by the medical profession and the nonprofessional press is much needed. Dr. Smith also makes no distinction between animal parasitology and bacteriology in his arrangement of subject matter and his topical discussions. The neglect of parasitology in premedical and clinical medical instruction has given a bacteriologic slant to the practice of medicine which all too often limits diagnosis and therapy.

The book opens with a chapter on the derivation of the parasitic mode of life from the predatory one. This is followed by a discussion of the various patterns of life cycle, all of which involve four important stages; namely, adjustment and adaptation to invasion, to multiplication, to emigration or passive discharge, and to transfer to fresh hosts. These four demands are met in various ways, each matched against the resisting powers of the host.

The second chapter deals with aberrant parasitisms, which are not regarded as insignificant accidents but rather as the most important factors in the evolution of both parasitism and disease. Aberrance is the adventurous element in the life of the parasite, which leads either to death or to new conquests. Establishment in new hosts paves the way for the formation of new races and varieties, for the new host modifies and molds the invader until a new equilibrium has been established. Aberrance of parasites is furthermore responsible for the

development of disease whenever they reach a more yielding host. Most epidemics or pandemics are probably due to strayed parasites. A study of epizootics among small experimental animals kept together in large numbers tends to show that such diseases are most virulent at the start and gradually change their characters, becoming less infectious, more chronic, nonfatal, and topographically altered as regards the incidence of lesions. The epidemic is probably the first sign of a straying of parasites from either near or more distantly related hosts to new hosts not previously infected, or from an immune group to a susceptible group of the same species or race.

The chapter on the host-parasite conflict analyzes the factors in the battle that ensues when the parasite grows or multiplies within the host. "This is the stage to which medical science has given most attention, and it is the one in which disease as well as cure from disease is generated." Here is found a discussion of racial susceptibility, endemicity, infantile susceptibility, bactericidal ferments and their sources, alexin and opsonin, and other antialien activities of the host and, on the other hand, of the toxins, aggressins, capsules and other envelops of bacteria and of the cuticula of worms and the envelops of their ova. The cuticula is nondigestible. The living cells of the parasite are protected from the digestive ferments of the host by an intracellular antidigestive mechanism, which death of the parasite disrupts. The patterns of host-parasite relations are modified by differences in host species, races and individuals, and by their environment, by variations in parasites induced by the environment of artificial cultures, by differences due to stages of adaptation in the evolution of the parasitic mode of life, and by differences due to naturally occurring or artificially induced aberrant parasitism. Moreover, there is no generally uniform order in which the various antialien activities are brought out by the reciprocal stimulation of host and parasite. All one can do is to catalogue these activities in the individual and utilize them in the comparative study of types of parasitism. The forces of the host tend in one direction, destroying or rendering harmless the parasite. The parasite has its mechanism set for multiplication or increase in size. Both involve processes of digestion and assimilation. The host, however, is not dependent on the products of such digestion, whereas the parasite is completely dependent. The host by simply checking the parasite's growth activities has protected itself sufficiently. The parasite, on the other hand, must be able to overcome the antialien forces of the host, in at least a circumscribed territory, by destructive or neutralizing processes while it increases in numbers or develops to maturity. The parasite's ammunition consists of a variable number of factors, such as metabolic products or toxins and such as are released by disintegration of some of the parasites, also special metabolic products of the host species which may be favorable to the multiplication and growth of parasites, enveloping protective substances, capsules of varying degrees of consistency and reproductive activities, and finally ectoplasms or limiting membranes of specific permeability or resistance to digestion. The host, on the other hand, has certain general lytic or digestive powers and the capacity to develop at varying rates antibodies that neutralize toxins and such as paralyze the growth activities of the parasite and envelop and immure it.

Phagocytosis has played a part in the evolution of parasitism, because there has been interposed between the general antialien activities of the host and the vulnerable evolving parasite a new substance in the form of a protecting capsule or of a new state of the surface of the parasite. This demanded the formation of specific antibodies by the host and also the adaptation of certain normally phagocytic cell groups or the internment and gradual destruction of the parasite.

In the chapter on variation and mutation in parasitic organisms, the author states that the "work of the past generation has revealed a fundamental stability of the characters of microorganisms with restricted variability" and is somewhat noncommittal on the validity of the ultravisible forms of the bacteria.

In his theoretical discussions he accepts natural selection, but throughout the book he is a thoroughgoing Lamarckian with regard to potency of environmental factors in the evolution of parasitism and host-parasite relations.

In the chapter on survival and host-to-host movement one finds a survey of this interesting aspect of parasitism, with a discussion of antepartum and postpartum transfer through the placenta and milk respectively; of the transfer of antibodies in the early colostrum of the cow in the first two days and the persistence of the protection for only several months; of the inheritance of parasites in insects by way of the ovum; of infection by droplet from the respiratory tract, by insect vectors, and by contamination; of the function of the carrier in the spread and maintenance of communicable diseases; and of the relation to human diseases of domesticated animals and others, such as rats and other rodents associated with man.

The chapters on epidemiology and on the ultilization of discoveries contain a review of the relations of epidemics to civilization and an assessment of values of the achievements to date both for public health and sanitation and for personal hygiene.

This book should be read and digested not only by every public health administrator, physician and nurse but also by the medical practitioner. The layman seeking a general picture of the relation of communicable diseases to society will find the book readable and informing. The biologist will appreciate the comprehensive picture which it presents of disease in its relation to the organism and to the evolutionary process.

How to Use a Medical Library: A Guide to Research for Practitioners, Research Workers and Students. By Leslie T. Morton, Associate of the Library Association. Boards. Price, 2s. 6d. Pp. 70. London: John Bale, Sons & Danielsson, Ltd., 1934.

The author of this volume is assistant in the Library of the Royal College of Medicine. He is a firm believer in the idea that those who use libraries should prepare their own bibliographies. The author describes the development of various medical indexes and discusses uses of these indexes and the location of periodical literature, and then the compilation of medical bibliographies. He also describes the methods of using card catalogues in medical libraries. Two appendixes list the available indexes and abstracting journals and the medical libraries of Great Britain. There is also a bibliography of works on the consultation of medical literature.

Death Rates by Occupation Based on Data of the U. S. Census Bureau, 1930. Edited by Jessamine S. Whitney, Statistician, National Tuberculosis Association. Boards. Price, $1. Pp. 32. New York: National Tuberculosis Association, 1934.

All who are interested in the trend of death rates by occupation or who have use for comparative data pertaining to the relative importance of certain specified causes of death in selected occupations will welcome these compilations. Although the tables do not contain data covering the entire United States, accurate figures are presented for a limited area. This volume may well serve as an introduction to a complete tabulation of census figures on a subject that is vital in any study of industrial hygiene and workmen's compensation. If death rates according to occupation can be used to some degree to indicate the relative risk in various industries and serve to stimulate more scientific and concerted efforts to reduce these hazards, the preparation of these data will have served a definite purpose in individual and community welfare.

Lumbalanästhesie in der Geburtshilfe und Gynäkologie mit besonderer Berücksichtigung der Biochemie des Liquors und der Blutliquorschranke. Von Dr. Ernst Preissecker, Assistant der II. Univ.-Frauenklinik Wien (Prof. W. Weibel). Mit einem Vorwort von Prof. Dr. W. Weibel. Cloth. Price, 7.50 marks. Pp. 76, with 5 illustrations. Vienna: Wilhelm Maudrich, 1934.

In this book the author reviews the history of spinal anesthesia, the biochemistry of the cerebrospinal fluid, the pharmacology of the drugs used for spinal anesthesia, the technic of lumbar puncture and spinal anesthesia, the use of this form of anesthesia in obstetrics and in gynecology, and the effect of spinal anesthesia on the intermediary metabolism. He advises against the use of morphine and other alkaloids preliminary to the use of spinal anesthesia because all alkaloids depress the respiratory center. He employed nupercaine in 1,200 cases and prefers the sitting posture for the insertion of the anesthetic. However, in pregnant women near or at term, the lateral position must be employed. The sensitiveness of gravid women to spinal anesthetics is definitely increased, because during gestation there is a greater tendency toward bleeding, an

increased permeability of the blood vessels, a more ready transfer of material from the cerebrospinal fluid into the general circulation, a diminished pulmonary capacity, and a sudden filling of the splanchnic vessels after extraction of the child. In spite of this the author believes that spinal anesthesia is highly suitable for obstetric operations, especially cesarean sections. However, pregnant women who have cardiac disease should never be given spinal anesthesia. The author maintains that spinal anesthesia cannot supplant twilight sleep because it is too risky. In the series of gynecologic cases reported, satisfactory anesthesia was induced in 91.8 per cent. To the rest, ether had to be given. This book should prove valuable to all who are interested in spinal anesthesia.

A Doctor Studies Crime. By Perry M. Lichtenstein, M.D., LL.B., Medical Assistant, District Attorney, County of New York. Cloth. Price, $3. Pp. 263. New York: D. Van Nostrand Company, Inc., 1934.

The author of this volume was for over eighteen years resident physician of the Tombs in New York and for nearly three years medical assistant of the district attorney. His discussion of crime is therefore based on study of several hundred thousand people accused of criminal acts. His book is enlivened by many anecdotes of the great and near great criminals with whom he has had contact. The chapters of the book discuss the prison physician, narcotic addiction, the relationship of mental and moral defects and of insanity to crime, the uses of probation, the detention prison, court procedure and the penal institution. This is a first hand account of the work of the prison physician, which may be read with interest by every one interested in crime and its detection and also by those interested in prison reform.

Common Skin Diseases. By A. C. Roxburgh, M.A., M.D., B.Ch., Physician in Charge of the Skin Department and Lecturer on Diseases of the Skin, St. Bartholomew's Hospital. Second edition. Cloth. Price, 16s. Pp. 369, with 136 illustrations. London: H. K. Lewis & Company, Ltd., 1934.

This edition has been enlarged by the inclusion of chapters on congenital disorders of the skin, atrophies and scleroses, vesicular and bullous eruptions and erythrodermias. The addition of a goodly number of reproductions of clinical photographs and photomicrographs has enhanced the attractiveness of the book. The point of view of the general practitioner has been preserved by emphasis on differential diagnosis and by omission of those methods of treatment that ordinarily are to be had only in specialists' offices. It is unfortunate that the formulas are not given in the metric system as well as in the older one. Taken as a whole one must give praise to the printers for the excellence of the heavy paper used, for the attractive maroon-colored gold-stamped leather binding, and to the author for his careful, conservative and concise selection of material.

Odoratus Sexualis. By Dr. Iwan Bloch. A Scientific and Literary Study of Sexual Scents and Erotic Perfumes. Cloth. Price, $5. Pp. 274. New York: American Anthropological Society, 1933.

Here is a reprint in English at a very high price of a rather obsolete essay on the relationship of odor to sex. It has long been understood that human beings possess odors which are quite distinctive and that perfumes of various types have been associated with sexual stimulation. The author discusses these matters from both ethnological and biologic points of view.

Código de deontología médica. Por Louis Alonso Muñoyerro, presbítero, auditor fiscal del Supremo Tribunal de la Rota Española. Prólogo del Dr. A. Vallejo Nágera. Cloth. Pp. 250. Madrid: Ediciones Fax, 1934.

In this day of codes it is interesting to see what a really thoroughgoing code may be, for under this title, filling some 130 duodecimo pages, there is enunciated a code of medical ethics that leaves no aspect of the physician's life untouched. Three chapters are devoted respectively to the intellectual, moral and physical qualifications of the physician. His relationships to the sick, to society and to the profession are minutely analyzed. All matters pertaining to marriage, birth control, sterilization and artificial impregnation are treated from the strictly orthodox point of view, as might be expected. The author is a doctor of sacred theology and canon law; also a member of the Supreme Tribunal of the Spanish Rota.

One Hour of Medical History. Volume III. By Benjamin Spector, M.D., Director. Cloth. Price, $2. Pp. 181, with illustrations. Boston: Tufts College Medical School, 1934.

The Tufts College Medical School has presented each year a pageant of the history of medicine. The first two have already been published in book form. With increasing experience the material becomes more finished. Students are chosen from the second, third and fourth years who make an earnest effort to bring to life the characters they impersonate. The present volume carries the reader and the listener from Imhotep to Roentgen. The book is nicely illustrated. The essays, while brief, are highly suggestive.

Anatomy of Animal Types for Students of Zoology. By E. A. Briggs, D.Sc., Assistant Professor of Zoology in the University of Sydney. Cloth. Price, 10/6. Pp. 250. Sydney, Australia: Angus & Robertson, Ltd., 1934.

Most of the textbooks about zoology are concerned with species not available in Australia. For this reason Prof. E. A. Briggs has prepared a manual of zoology especially for the Australian student, dealing with vertebrates and invertebrates that are used by the students in that country. His book will, of course, be useful to such students as a textbook and to those in other countries as a work of reference.

Biographical History of the Members of the McLean County Medical Society and Other Physicians Who Have Practiced Medicine in McLean County, 1854-1934. Paper. Pp. 79, with illustrations. Bloomington, Illinois: The Society, [n. d.].

On March 20, 1854, fourteen physicians assembled in Bloomington, Ill., to organize the McLean County Medical Society. On the fiftieth anniversary, in 1904, the society requested one of its charter members, Dr. C. R. Parke, then of Louisville, Ky., to write a history of the medical society to be included in a history then being prepared by the McLean County Historical Society. The brief history prepared by Dr. Parke is the opening chapter in this small volume. It is followed by the original constitution of the McLean County Medical Society and by the revised constitution, which went into effect Dec. 1, 1904. There is a list of all the presidents and secretaries and a brief bibliography of all the members from the organization of the society down to the present. The history closes with a brief account of several hospitals in Bloomington and of the eightieth anniversary and banquet of the McLean County Medical Society, held May 8, 1934.

Die Werke des Hippokrates: Die hippokratische Schriftensammlung in neuer deutscher Übersetzung. Herausgegeben von Dr. med. Richard Kapferer. Unter Mitwirkung von Prof. Dr. Georg Sticker, u. a. Teil 1: Sitten- und Standeslehre für Aerzte. Teil 2: Die Alt(bewährt)e Heilkunst/Die Kunst. Die hippokratische Schriftensammlung in neuer deutscher Übersetzung. Boards. Price, 98.75 marks, per set. (Subskriptionspreis). Pp. 59; 59. Stuttgart & Leipzig: Hippokrates-Verlag G. m. b. h., 1934.

The author offers a new translation into German of the works of Hippocrates. It is to be published in parts with a hope of bringing physicians back to the hippocratic conception of diseases and its control.

Atlas of External Diseases of the Eye. By Humphrey Neame, F.R.C.S., Hon. Ophthalmic Surgeon, Royal London Ophthalmic Hospital. Cloth. Price, $5. Pp. 110, with 51 illustrations. Philadelphia: P. Blakiston's Son & Company, Inc. 1934.

This is an atlas containing fifty-one colored drawings of diseases of the lids and the eyeball. Accompanying each plate and opposite it is a brief discussion of the condition giving the signs, symptoms, diagnosis, etiology, pathology, prognosis and treatment of the conditions. Most of the plates are quite good and it is possible to make a diagnosis from the pictures alone. The book should be of value to the student and the general practitioner.

Les ordonnances du médecin praticien: 256 répertoires de thérapeutique clinique. Par MM. S. Abbatucci et al. Third edition. Paper. Price, 50 francs. Pp. 526. Paris: Masson & Cie, 1934.

This collection of highly practical brief articles on the nonsurgical treatment of diseases, first suggested by Martinet, has been brought down to date in this revised edition by incorporation of recent progress. It is neither a treatise on therapeutics nor a mere formulary, but a collection of outlines of treatment

sketched by experts in their respective lines and made applicable to current clinical and social conditions. It is decidedly a book that the general practitioner who understands French would find a good investment.

Medicolegal

Medical Practice Acts: Injunction to Restrain Unlicensed Practice.—The state of Arizona, on the relation of the attorney general, filed a bill of complaint against A. T. Smith to enjoin him from practicing medicine and surgery without first having obtained a license to do so. The trial court sustained Smith's demurrer to the complaint and the state appealed to the Supreme Court of Arizona.

The complaint alleged that Smith was engaged in the practice of medicine and surgery without a license, that he was unskilful and uninformed in that practice, that he did not possess the moral and professional qualifications prescribed therefor, that his continuous and persistent practice constituted a public nuisance, detrimental to the public welfare and dangerous to the public health, and contrary to and against the public policy of the state. The regulation of the practice of medicine and surgery by the state has for its purpose, said the court, the protection of the public health; and the attorney general, as a legal adviser of the state, may properly institute and prosecute a suit against those who fail or refuse to comply with the requirements of the medical practice act.

When the defendant demurred to the complaint he admitted as true the facts pleaded therein. The difficult question in this case, said the Supreme Court, is whether, in the absence of specific statutory authority, a person may be enjoined from committing a crime for which the legislature has prescribed a punishment. The general rule is that the courts will not enjoin one from committing a crime. As an exception to this rule, however, it is generally held that an injunction will be granted to restrain acts constituting a public nuisance, if they affect the civil or property rights or privileges of the public, or affect the public health, whether such acts be denounced as crimes or not. Section 4693, Revised Code of Arizona, 1928, provides that "anything which is injurious to health . . . is a public nuisance," and in the present case the state based its right to an injunction, in part, on the allegation that the acts of the defendant, because of his lack of training and education, constituted a public nuisance affecting the public health. It is obvious, observed the court, that one who knows little or nothing of the human body and its reactions is unable intelligently and wisely to diagnosticate or prognosticate human ills, or to adopt sanitary means to prevent their spread or to effect their cure. If in fact, continued the court, the defendant was unskilful and uninformed, as alleged in the complaint, and daily treated people for their ills, it was not only probable but very likely that he was injuring the health of those he treated rather than helping them. His acts were consequently injurious to health and a menace to life.

The court did not think, however, that the unlicensed practice of medicine and surgery was per se a nuisance, as seems to have been held in *Kentucky State Board of Dental Examiners* v. *Payne*, 213 Ky. 382, 281 S. W. 188, and in *State* v. *Anderson*, 6 Tenn. Civ. App. 1. In the opinion of the court, a license does not add to a person's qualifications. It only shows that the holder has complied with the law. His skill and ability as a practitioner would be the same before as after he secured the license. A person having a license from the proper authorities would be presumed to be qualified to practice, and, in a criminal prosecution for violating the law requiring a license before practicing, the absence of such a license would give rise to an unrebuttable presumption of disqualification. But, observed the court, in a proceeding for an injunction based on acts alleged to be injurious to health by reason of unskilfulness, ignorance and incompetence, the state must make out its case. In the present case, the complaint alleged that the acts of the defendant were injurious to health and constituted a public nuisance. These allegations were not only not denied but were admitted by the demurrer. The Supreme Court concluded therefore that the injunction should have been granted. The judgment of the trial court was accordingly reversed and the cause remanded, with directions that a permanent injuction be issued restraining the defendant from the further practice of medicine and surgery without a license. Subsequently, however, on a rehearing of the appeal, the Supreme Court revised its order and directed the trial court to overrule Smith's demurrer and permit him to make further answer to the complaint.—*State ex rel. La Prade, Atty. Gen., v. Smith (Ariz.), 29 P. (2d) 718; 31 P. (2d) 102.*

Malpractice: Death Resulting from Chiropractic Treatment for Headache.—The defendant, a chiropractor, undertook to treat Mrs. Thornton for a chronic headache by giving her so-called chiropractic adjustments daily. At the end of the fifth "adjustment" the patient complained of excruciating pains in her neck and head and the chiropractor called a nonsectarian practitioner. A blood vessel in the patient's brain seems to have been ruptured and the patient died about two weeks later. Attributing the death to malpractice on the part of the chiropractor, the plaintiff, her husband, sued the chiropractor. There was a judgment for the plaintiff and the chiropractor appealed to the Supreme Court of Florida.

For a plaintiff to recover in a malpractice suit, said the Supreme Court, he must show two things; namely, (1) that the defendant was unskilful or negligent and (2) that that want of care or skill resulted in injury to the plaintiff. The absence of either of these two conditions will defeat recovery. While an unfortunate result raises no presumption of negligent treatment, negligence may be inferred from circumstances. For the circumstances to raise a fair presumption of negligence, they must of necessity not only be consistent with the theory that the injury resulted from negligence but also be inconsistent with the theory that the injury resulted from any other cause which might just as reasonably and logically be established by the circumstances. Applying these general principles to the facts of this case, the court said:

> The jury in the case decided that the treatment administered by the doctor [chiropractor] produced the patient's death, which was caused by a ruptured blood vessel in the brain. This conclusion was evidently arrived at from the evidence of physicians and surgeons, who said that the rupture was caused by violence, and from the testimony of the defendant himself that the "adjustment" to which he submitted the patient, if properly made, could not have caused the rupture. That the rupture was caused by the adjustment was evidenced by the fact that the patient went to the doctor's [chiropractor's] rooms for a treatment like that which she had before received, and, while under the treatment, suddenly suffered the shock which resulted in severe pain and subsequent unconsciousness.

The Supreme Court accordingly affirmed the judgment in favor of the plaintiff.—*Foster v. Thornton (Fla.), 152 So. 667.*

Society Proceedings

COMING MEETINGS

Academy of Physical Medicine, New York, Oct. 30-31. Dr. Arthur H. Ring, 163 Hillside Avenue, Arlington, Mass., Secretary.

American Society of Tropical Medicine, San Antonio, Texas, November 14-16. Dr. Henry E. Meleney, Vanderbilt University School of Medicine, Nashville, Tenn., Secretary.

Association of American Medical Colleges, Nashville, Tenn., Oct. 29-31. Dr. Fred C. Zapffe, 5 South Wabash Avenue, Chicago, Secretary.

Central Association of Obstetricians and Gynecologists, New Orleans, Nov. 1-3. Dr. Ralph A. Reis, 104 South Michigan Boulevard, Chicago, Secretary.

Central Society for Clinical Research, Chicago, Nov. 2-3. Dr. Lawrence D. Thompson, 3720 Washington Boulevard, St. Louis, Secretary.

Inter-State Postgraduate Medical Association of North America, Philadelphia, November 5-9. Dr. W. B. Peck, 27 East Stephenson Street, Freeport, Ill., Managing-Director.

Omaha Mid-West Clinical Society, Omaha, Oct. 29-Nov. 2. Dr. Joseph D. McCarthy, 107 South 17th Street, Omaha, Secretary.

Pacific Coast Society of Obstetrics and Gynecology, Oakland and Del Monte, Calif., November 21-23. Dr. Clarence A. De Puy, 230 Grand Avenue, Oakland, Secretary.

Puerto Rico, Medical Association of, Santurce, Dec. 14-16. Dr. Julio R. Rolenson, Box 3403, Santurce, Secretary.

Radiological Society of North America, Memphis, Tenn., December 3-7. Dr. Donald S. Childs, 607 Medical Arts Building, Syracuse, N. Y., Secretary.

Southern Medical Association, San Antonio, Texas, November 13-16. Mr. C. P. Loranz, Empire Building, Birmingham, Ala., Secretary.

Southern Surgical Association, Sea Island, Ga., Dec. 11-13. Dr. Robert L. Payne, 142 York Street, Norfolk, Va., Secretary.

Western Surgical Association, St. Louis, December 7-8. Dr. Albert H. Montgomery, 122 South Michigan Boulevard, Chicago, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers to THE JOURNAL in continental United States and Canada for a period of three days. Periodicals are available from 1925 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

American Journal of Medical Sciences, Philadelphia

188: 301-440 (Sept.) 1934

Social Incidence of Rheumatic Heart Disease: Statistical Study in New Haven School Children. J. R. Paul, Elizabeth R. Harrison, R. Salinger and G. K. DeForest, New Haven, Conn.—p. 301.
*Recurrences in Pneumococcus Pneumonia. M. Finland and A. W. Winkler, Boston.—p. 309.
*Cytology of Pleural Effusions in Pneumonia Studied with Supravital Technic. T. F. M. Scott, Baltimore, and M. Finland, Boston.—p. 322.
Occurrence of Myelocytes in Peripheral Blood in Lobar Pneumonia. D. J. Stephens, Rochester, N. Y.—p. 332.
Evanescent Effect of Intratibial Injections of Bacillus Welchii Toxin in Rabbits. L. J. Goldwater, J. E. Connery and H. Heimann, New York.—p. 339.
Lack of Effect of Liver Treatment on Circulating Reticulocytes in the Pigeon. H. Heimann, J. E. Connery and L. J. Goldwater, New York.—p. 343.
Spontaneous Rupture of Heart Simulating Surgical Abdominal Disease. H. A. Salzmann, Philadelphia.—p. 347.
*Enlargement of Heart Due to Abnormal Glycogen Storage: In von Gierke's Disease. W. Antopol, J. Heilbrunn and L. Tuchman, New York.—p. 354.
Effect of Elevated Metabolism on Heart of Frizzle Fowl: II. Increased Ratio of Heart to Body Weight. E. P. Boas, New York, and W. Landauer, Storrs, Conn.—p. 359.
Familial Cleidocranio Dysostosis. Julianna R. Tatum, Philadelphia.—p. 365.
Sympathogonioma of Adrenal. H. L. Peters and B. Horn, Bridgeport, Conn.—p. 372.
Treatment of Bichloride of Mercury Poisoning: Study of Forty-Six Cases. W. B. Porter and C. E. Simons, Richmond, Va.—p. 375.
*Study of Auricular Fibrillation Following Operations for Goiter. A. C. Ernstene and B. E. Mulvey, Cleveland.—p. 382.
Electrocardiographic Changes Produced by Injuries of Various Parts of Ventricles. H. Korey and L. N. Katz, Chicago.—p. 387.
Arteriovenous Fistula of Renal Vessels. E. W. Hollingsworth, Hines, Ill.—p. 399.
Large Doses of Tuberculin in Testing Guinea-Pigs Inoculated for Diagnostic Purposes. T. B. Magath, Rochester, Minn.—p. 403.
So-Called "Primary" Tuberculosis of Muscle. H. Milch, New York.—p. 410.

Recurrences in Pneumococcic Pneumonia.—Finland and Winkler present a study of fifty-seven cases of recurrent attacks of pneumonia associated in each instance with serologically identified pneumococci. An analysis of the major features of the early attacks and of the recurrence fails to indicate any marked change in the local or type specific susceptibility. The distribution of types of pneumococci and of the sites of the pulmonary lesion, in both the early and the late attacks, was similar to that usually observed in pneumococcic pneumonia. A larger number of cases had more extensive and "atypical" lesions during the recurrent attack. Specific serum therapy in the first attack in general had no marked effect on the character of the recurrence. Early recurrences with the same type, however, are more frequent among the cases treated with serum.

Cytology of Pleural Effusions in Pneumonia.—Scott and Finland used the supravital technic described by Forkner (a modification of the methods of Simpson and Sabin and their associates) to study the cytology of fifty-three pleural fluids obtained from thirty-two patients having pneumococcic lobar pneumonia. The cellular content of the infected fluids consisted almost exclusively of polymorphonuclear neutrophils in various stages of degeneration. In uninfected fluids the predominating cells, in the beginning, were active polymorphonuclear neutrophils, but these decreased in number during the first week, at which time monocytes and macrophages appeared in the fluid. Later in the disease, after crisis had taken place, lymphocytes began to appear in these sterile fluids. Moderate to marked eosinophilia was noted in three cases. This occurred during the third week or later after the onset of the pneumonia.

Enlargement of Heart Due to Abnormal Glycogen Storage.—Antopol and his co-workers report a case of glycogenosis confirmed by necropsy. They state that deposits of glycogen may occur in the liver, kidneys, brain, heart, blood vessels, muscles and organs of internal secretion. The clinical picture depends on the sites of deposition and on the extent to which the vital processes of the affected tissues are interfered with. So far three main symptom groups are known, due to preponderance in the liver and the kidneys, in the heart and the blood vessels or in the brain. The first is the best known and possibly the largest group—the hepatonephromegalia glycogenica of von Gierke. The second group—that with cardiac hypertrophy—gives a clinical picture which, in the absence of proper chemical and histologic studies, may be confounded with the so-called idiopathic hypertrophy of the heart, as pointed out by Pompe. It is possible that many of the cases formerly classified as idiopathic hypertrophy belong to the von Gierke type of disease with enlarged heart and that rhabdomyomas are localized collections of fibers rich in glycogen, due possibly to focal disturbance in the metabolism of glycogen. In many cases of the so-called idiopathic hypertrophy vacuoles have been noted in the cardiac muscle but were not explained, and their association with large livers and enlarged kidneys is frequent. The third group, i. e., with cerebral symptoms due to glycogen deposits in the brain and spinal cord (Kimmelstiel) makes necessary a review of all poorly understood cerebral conditions in children in order to determine whether some of them are not related to the effect of abnormal glycogen storage.

Auricular Fibrillation After Goiter Operations.—According to Ernstene and Mulvey, sixteen (7 per cent) of 213 patients having hyperthyroidism had auricular fibrillation during the preoperative period, while postoperative auricular fibrillation developed in thirty-one (16 per cent) of the 197 who had normal rhythm before operation. The arrhythmia was present before operation in two of 192 patients who had adenomatous goiter without hyperthyroidism and developed after operation in four. The age of the patient, type of goiter and duration of hyperthyroidism appear to be the most important factors predisposing to the development of postoperative auricular fibrillation. The degree of elevation of the basal metabolic rate is of little significance. The immediate increase in the rate of metabolism following operation probably is the essential factor responsible for the initiation of the arrhythmia. Postoperative auricular fibrillation is more common in thyrotoxic patients having an adenomatous goiter than in those with hyperplastic goiter. This difference cannot be explained entirely by differences in the ages of the patients belonging to the two groups. The long duration of thyroid enlargement in the majority of patients having adenomatous goiter may favor the gradual development of myocardial damage, possibly as the result of repeated or prolonged periods of low grade, unrecognized hyperthyroidism. Postoperative auricular fibrillation generally begins during the first sixty hours after operation. It rarely causes circulatory embarrassment, and normal rhythm is reestablished spontaneously within forty-eight hours.

American Journal of Ophthalmology, St. Louis

17: 683-786 (Aug.) 1934

Principles of Modern Surgery in Ophthalmology. J. M. Wheeler, New York.—p. 683.
Infantile Glaucoma. J. F. Hardesty, St. Louis.—p. 689.
Progressive Exophthalmos in Thyroid Disease: Report of Malignant Case. M. Goldenburg, Chicago.—p. 692.
Operative Treatment of Cataracts. A. B. Bruner, Cleveland.—p. 699.
Tangent Rule as a Diagnostic Instrument. R. K. Simpson, Randolph Field, Texas.—p. 705.
Low Fusion Convergence as a Factor in Reading Disability. T. H. Eames, West Somerville, Mass.—p. 709.
Kinetic Velonoscopy. P. Good, Aurora, Ill.—p. 711.
A View into the Ophthalmology of Galen. B. Chance, Philadelphia.—p. 718.
Symmetric Incomplete Annular Scotoma of Tobacco Origin Without Enlargement of the Blind Spot. E. Krimsky, Brooklyn.—p. 722.
Microphakia and Spherophakia with Glaucoma. T. M. Shapira, Chicago.—p. 726.
Effect of Diet and Vitamins on Trachoma. C. E. Rice, R. Sory, J. E. Smith, P. E. Faed and A. A. Drake, Rolla, Mo.—p. 735.
Vasomotor System in Retinal and Cerebral Vascular Lesions. D. Kravitz, Brooklyn.—p. 741.

American Journal of Physiology, Baltimore

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Changes of Carbohydrate Metabolism of Heart Following Coronary Occlusion. H. E. Himwich, W. Goldfarb and L. H. Nahum, New Haven, Conn.—p. 403.

Nutritional Significance of Vitamin A Throughout Life Cycle. Esther L. Batchelder, New York.—p. 430.

"Fat Metabolism Hormone" and Hyperglycemia. B. Harrow, I. M. Chamelin and A. Mazur, New York.—p. 436.

Studies on Nervous System in Deficiency Diseases: Experimental Black Tongue. H. M. Zimmerman, G. R. Cowgill, W. W. Bunnell and Margaret Dann, New Haven, Conn.—p. 440.

What Constitutes Lethal Reduction of Temperature? F. K. Jackson and A. Alonge, Burlington, Vt.—p. 447.

Studies on Action of Alkali Iodides. J. J. Westra.—p. 450.

Permeability of Blood Capillaries to Lipoids. A. Marble, Madeleine E. Field, C. K. Drinker and Rachel M. Smith, Boston.—p. 467.

Hypoglycemia Hypophysiopriva. W. Mahoney, New York.—p. 475.

Spiral Propulsion of Bolus in Intestine. P. E. Reid, A. C. Ivy and J. P. Quigley, Chicago.—p. 483.

Clearance of Creatine in Dog and Man. R. F. Pitts, New York.—p. 532.

Influence of Neutral Sodium Salt Solutions on Chemical Stimulation. I. Chao, Chicago.—p. 550.

Cold Stimulation and Influence of Neutral Sodium Salt Solutions on Cold Stimulation. I. Chao, Chicago.—p. 561.

Composition of Edema Fluid and Lymph in Edema and Elephantiasis Resulting from Lymphatic Obstruction. C. K. Drinker, Madeleine E. Field, J. W. Helm and O. C. Leigh Jr., Boston.—p. 572.

Effect of Histamine on Jejunal Secretion. A. L. Berndt and I. S. Ravdin, Philadelphia.—p. 587.

Annals of Otol., Rhinol. and Laryngology, St. Louis

43: 643-944 (Sept.) 1934

Effects of Ionization on Mucosa of Frontal Sinuses of Dogs. B. J. McMahon, St. Louis.—p. 643.

Meningitis Secondary to Otitic or Sinus Infection: Comprehensive Study of Meningitis Secondary to Otitic or Sinus Infection. Josephine B. Neal, H. W. Jackson and E. Appelbaum, New York.—p. 658.

Id.: Bacteriology of Meningitis Following Otitis Media and Related Infections. Anna W. Williams, New York.—p. 667.

Id.: Pathways of Infection in Suppurative Meningitis. A. A. Eggston, New York.—p. 672.

Id.: Present Status of Treatment of Meningitis. J. G. Dwyer, New York.—p. 689.

Id.: Forced Drainage for Treatment of Meningitis Secondary to Ear and Sinus Infections. L. S. Kubie, New York.—p. 692.

Pathology and Routes of Infection in Labyrinthitis Secondary to Middle Ear Otitis. L. W. Dean and Dorothy Wolff, St. Louis.—p. 702.

Differential Diagnosis in Labyrinthitis Secondary to Otitic Infections. S. J. Kopetzky, New York.—p. 718.

Operation for Removal of Carcinoma of Faucial Tonsil and Contiguous Parts. D. Macpherson, New York.—p. 727.

Hereditary Hemorrhagic Telangiectasia. K. M. Houser, Philadelphia.—p. 731.

Jacobson's Organ (Organon Vomeronasale, Jacobsoni): Its Anatomy, Gross, Microscopic and Comparative, with Some Observations as Well on Its Function. S. J. Pearlman, Chicago.—p. 739.

*Tonsillectomy in the Tuberculous: Incidence and Pathology of Tuberculosis of Tonsils in Adults. H. Newhart, S. S. Cohen and Charlotte C. Van Winkle, Minneapolis.—p. 769.

Infections of Temporal Bone with Secondary Manifestations. M. F. Jones, New York.—p. 779.

Parapharyngeal Space: Anatomic and Clinical Study. C. Hall, Los Angeles.—p. 793.

Efficiency of Antroscopic Examination of Maxillary Sinus. E. Simon, Albany, N. Y.—p. 813.

Pathology of Chronic Sinusitis in Children. W. Spielberg, New York.—p. 826.

*Etiologic Factors in Formation of Cholesteatoma. K. M. Day, Pittsburgh.—p. 837.

Lymphogranulomatosis and Its Significance in Diagnosis of Diseases of Waldeyer's Ring. I. M. Sobol, Nieshin, the Ukraine, U. S. S. R.—p. 851.

Tonsillectomy in Tuberculous Adults.—Newhart and his associates found that the incidence of tuberculosis of the tonsils in 112 tuberculous adults was 42 per cent. If the twelve cases without pulmonary tuberculosis were eliminated, the incidence would increase to 48 per cent. Serial sections of the excised tonsils would materially increase the incidence. This was demonstrated by a study of twenty pairs of tonsils, in four of which tuberculosis was found. These had previously been reported negative by the usual microscopic study. In a control series of 100 routine tonsillectomies, the incidence was 1 per cent, the positive case being found in a patient who had previously been treated for active pulmonary tuberculosis. Tuberculosis of the tonsil is a "latent" lesion, in that there is rarely enough destruction of the tonsillar substance to cause "gross" or ulcerative lesions. The tubercles in the tonsil are usually in close proximity to the cryptal epithelium. The tubercles are primarily epithelioid in type, with giant cells nearly always present. Caseation is found in about half the cases and is not marked. The tonsils, in the authors' opinion, become infected by tubercle-laden sputum secondary to the open tuberculous pulmonary lesion. No case of primary tonsillar tuberculosis could be demonstrated in their series. Tonsillectomy in the tuberculous, when the patients are carefully selected and prepared, safeguarded by a proper operative technic and given the postoperative care demanded by their condition, presents no special hazard that would justify failure to perform tonsillectomy when indicated.

Etiologic Factors in Formation of Cholesteatoma.—Day believes that the primary and major factor in the development and growth of cholesteatoma is the presence of moisture. The surface epithelium of the body does not tolerate moisture well, and the continued contact of moisture causes irritation and desquamation of epithelium. The squamous stratified epithelium, which grows into the tympanic cavity and gives rise to cholesteatoma, is surface epithelium. The desquamation of epithelium and formation of cholesteatoma are primarily due to the constant presence of moisture bathing the epithelium. The author states that only anhydrous solutions should be employed in the presence of cholesteatoma. Conservative treatment should be tried only in the absence of symptoms or signs of extension beyond the confines of the middle ear and mastoid. Cures can be obtained only if there is complete epidermization of the walls of the cavities. The presence of moisture will prevent cures and cause recurrences. This is especially true if there are granulations or if an open eustachian tube is present. Conservative treatment is rarely successful in young children because of tubal secretion. The early recognition and proper treatment of chronic otitic suppuration with cholesteatoma should obviate the need of radical surgery and prevent the serious complications that occur so commonly at present.

Archives of Dermatology and Syphilology, Chicago

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Dermatophytes: Natural Grouping Based on Form of Spores and Accessory Organs. C. W. Emmons, New York.—p. 337.

Sarcoma Idiopathicum Multiplex Haemorrhagicum (Kaposi): Variations from Usual Clinical Picture. J. R. Webster, Chicago.—p. 363.

Louis Adolphus Duhring: Great American Dermatologist. P. E. Bechet, New York.—p. 369.

*Cutaneous Rheumatic Nodules. W. A. Rosenberg, Chicago.—p. 377.

*Fungi of Blastomycosis and Coccidioidal Granuloma. Rhoda W. Benham, New York.—p. 385.

Cutaneous Leishmaniasis: Report of Two Cases. F. W. Roberts, New Haven, Conn.—p. 401.

Glossitis Rhombica Mediana: Report of Case with Results of Treatment. A. B. Abshier, New York.—p. 409.

Darier's Disease with Fatal Radium Dermatitis. J. González Urueña, Mexico City, Mexico.—p. 412.

Arsphenamine Dermatitis Resembling Pityriasis Rosea. S. Feldman and I. M. Lashinsky, New York.—p. 415.

American Distribution of Deaths from Cancer of Skin, Mouth and Breast. W. F. Petersen, Chicago.—p. 425.

Clinical Spectroscopy: Study of Biopsy Material from Patients Who Had Received Intravenous Injections of Silver Arsphenamine. L. E. Gaul and A. H. Staud, New York.—p. 433.

Cutaneous Rheumatic Nodules.—Rosenberg presents two cases of cutaneous rheumatic nodules with biopsies that occurred in adults. Histologic examination of a biopsy specimen of one of the cases showed that the epidermis was slightly thickened and the layer of keratohyalin well developed. Between the prickle cells were single cells, which were swollen with clear cytoplasm and pyknotic nuclei. The papillary layer of the cutis appeared loosened; the lymph vessels were dilated and the fibrocytes were swollen. There was slight acanthosis, and at the height of the tips of the rete pegs the cutis showed loose accumulations of small round cells, histiocytes and occasional plasma cells, which centered about capillaries with swollen endothelial cells. In the reticular layer of the cutis the edema and the perivascular infiltration were more marked, and the connective tissue trabeculae were often separated by rows of round cells which radiated from the cellular adventitia of the capillaries and the precapillary and postcapillary blood vessels. These vessels showed a slight thickening of the wall caused by a swelling and increase in the number of endothelial cells. The adventitial cells were swollen and more numerous than normal. There were similar infiltrations about the sweat

glands, which, however, were less marked than those about the blood vessels. In the subcutaneous fat tissue corresponding to the center of the infiltrated area was a small artery, the endothelial cells of which were so swollen that they resembled the epithelial lining of a gland. Sheets of desquamated endothelial cells with fibrin, leukocytes and round cells filled the lumen. The media stained pale, the muscle fibers were poorly differentiated and the nuclei were shrunken; the adventitia contained round cells and leukocytes, and similar cells were found between the adjacent fat cells. The small cutaneous nerves were surrounded by several rows of lymphocytes.

Fungi of Blastomycosis and Coccidioidal Granuloma.—Benham describes three types of mycotic infection—cryptococcosis, blastomycosis and coccidioidal granuloma. Each is a distinct disease etiologically. The infections may be diagnosed by the characteristic picture of the fungus in the lesions and this diagnosis may be confirmed by culture. The differential characteristics of the three fungi—Cryptococcus hominis, Blastomyces dermatitidis and Coccidioides immitis—are given for the sake of clearness. The author states that in addition to these three fungi there are at least seven others that may cause systemic infections with granulomatous lesions and appear in the infected tissue as rounded cells more or less resembling yeasts. Torula histolytica, Glenospora gammeli, Monosporium tulanense, Endomyces capsulatus, Geotrichum (Blastomycoides) dermatitidis, Scopulariopsis americana and probably other strains reported under various names seem indistinguishable from one or another of the three types described. For the recognition and identification of these fungi it is necessary to observe their morphologic characteristics both in the tissue of the host and in culture, their cultural characteristics, and, in the case of the first type, their serologic reactions.

Archives of Ophthalmology, Chicago

12: 307-472 (Sept.) 1934

Nature of Elementary and Initial Bodies of Trachoma. P. Thygeson, Iowa City.—p. 307.
Retinoblastoma: Report of Case with Complete Observations at Necropsy. M. Jaffe, New York.—p. 319.
*Operation to Control Glaucoma: Preliminary Report: H. Row, Indianapolis.—p. 325.
Diagnosis of Diseases of Eye: Value of History and Spontaneous Statements of Patient. H. G. A. Gjessing, Drammen, Norway.—p. 330.
Tubular Vision. R. C. Hamill, Chicago.—p. 345.
Experimental Studies on Swelling of Vitreous Gel and on Intra-Ocular Pressure. M. Cohen, J. M. Newell and J. A. Killian, New York.—p. 352.
Metastatic Carcinoma of Retina: Report of Case with Pathologic Observations. J. W. Smoleroff and S. A. Agatston, New York.—p. 359.
*Pressure on Optic Nerve by Carcinoma of Maxillary Sinus Extending into Cranial Cavity. I. Finkelman and S. Wick, Elgin, Ill.—p. 366.
Ligated Suture. P. C. Jameson, Brooklyn.—p. 377.
Nature of Photophobia. J. E. Lebensohn, with clinical assistance of J. Bellows, Chicago.—p. 380.
Amblyopia: Classification: Report of Cases. S. V. Abraham, Los Angeles.—p. 391.

Operation to Control Glaucoma.—After testing experimentally the possibility of establishing a fistulous tract from the anterior chamber through the suprachoroidal space and out through the sclera, for the control of intra-ocular hypertension, Row performed the horsehair insertion operation in a case of glaucoma secondary to the extraction of a cataract, in which the iris had become incarcerated in the incision, and in a case of bilateral absolute glaucoma, with constant and severe temporal headache. In this case both eyes had been operated on, the right eye once, by cyclodialysis, and the left eye twice, first by cyclodialysis, followed later by Elliot's operation, in an attempt to reduce the tension and thereby relieve the headache. Insertion of the horsehair was possible only after introducing a grooved spatula in the cyclodialysis tract. For this purpose a Knapp iris repositor was used, which acted as a guide to the hair as it was fed into the groove with a pair of tissue forceps. The possibility that sympathetic ophthalmia might be induced by this operation must not be overlooked. The fact that the operation opens a natural line of cleavage between the sclerotic and the choroid makes it incomparable to the violent, lacerating type of injury, perforating usually all three coats of the eye, which so frequently precedes the establishment of sympathetic ophthalmia. The author recommends a trial of the horsehair inclusion procedure in cases of primary bilateral absolute glaucoma. To his knowledge there is no other nonmutilating operation that offers any degree of success in such cases. Disregarding the consideration of sympathetic ophthalmia and assuming that by this procedure a sinus tract is opened from the anterior chamber back through the suprachoroidal space and thence into the deep orbital tissues, well covered and protected by Tenon's capsule, the possibility of late infection, as in other operations establishing a fistulous tract, is practically eliminated.

Carcinoma of Maxillary Sinus Extending into Cranial Cavity.—Finkelman and Wick report a case of a transitional cell carcinoma of the maxillary sinus extending into the cranial cavity. The development of the signs and symptoms in this case was at first due to the tumor near its origin. Later, with extension of the tumor into the cranial cavity, the patient complained of failing vision (optic atrophy and choked disk). The mental symptoms were probably a result of increased intracranial pressure. Neuropathologic examination of the brain and eye revealed arteriosclerotic changes in the brain, optic atrophy and disappearance of the ganglion cell layer of the retina.

Journal of Clinical Investigation, New York

13: 725-832 (Sept.) 1934

Effect of Coronary Occlusion on Initial Phase of Ventricular Complex in Precordial Leads. S. Bellet and C. G. Johnston, Philadelphia.—p. 725.
Influence of Protein Intake on Urea Clearance in Normal Man. W. Goldring, L. Razinsky, M. Greenblatt and S. Cohen, New York.—p. 743.
Effects on Renal Activity of Oral Administration of Phlorhizin in Man. W. Goldring, with technical assistance of Catherine Welsh, New York.—p. 749.
Renal Excretion of Xylose. R. Dominguez and Elizabeth Pomerene, Cleveland.—p. 753.
*Characteristics of Synovial Fluid in Gonococcic Arthritis. W. K. Myers, C. S. Keefer and W. F. Holmes Jr., Boston.—p. 767.
Urinary Excretion of Iodine: I. Loss of Iodine in Urine Following Thyroidectomy. G. M. Curtis and F. J. Phillips, Columbus, Ohio.—p. 777.
Therapeutic Effect of Total Ablation of Normal Thyroid on Congestive Heart Failure and Angina Pectoris: IX. Postoperative Parathyroid Function: Clinical Observations and Serum Calcium and Phosphorus Studies. D. R. Gilligan, D. D. Berlin, M. C. Volk, B. Stern and H. L. Blumgart, Boston.—p. 789.
*Observations on Treatment of Pellagra. T. D. Spies, Cleveland.—p. 807.
Radiation of Heat from Human Body: IV. Emission, Reflection and Transmission of Infra-Red Radiation by Human Skin. J. D. Hardy and C. Muschenheim, New York.—p. 817.

The Synovial Fluid in Gonococcic Arthritis.—In studying the synovial fluids from forty cases of gonococcic arthritis, Myers and his associates found that: 1. When the joints became involved as a result of a gonococcic infection, the synovial fluid was either infected or noninfected. In either case the fluid had the characteristics of an exudate as judged by both the total protein and cell content. 2. The total synovial fluid cell count was increased in both types of fluid, but, as a rule, it was somewhat higher in the infected fluids. There were, however, wide variations. 3. The differential cell count was of greater importance than the total cell count in the two groups of cases. In practically all, the polymorphonuclear cells predominated. In the noninfected fluids, the clasmatocytes, monocytes and lymphocytes were present in much larger numbers than in the infected fluids. 4. The nonprotein nitrogen content of the synovial fluid was the same as that of the blood regardless of the presence of organisms or of a high cell count. 5. The sugar content of the synovial fluid varied with the level of the blood sugar, the number of leukocytes and the presence of bacteria. Of these factors the first two were of greater importance than the third. 6. The results of gonococcus complement fixation tests on the synovial fluid and blood were in agreement. 7. The bacteriologic, cytologic and serologic tests were of the greatest value in providing information of diagnostic value. 8. The chemical examination of the fluid revealed no information of diagnostic importance. 9. While the prognosis, as far as complete recovery was concerned, was poor, the presence of micro-organisms and a high leukocyte count were more often followed by chronic disease of the joints than when there was a low leukocyte count and a sterile fluid.

Treatment of Pellagra.—Spies used autoclaved yeast, desiccated hog stomach and parenteral liver extract in the treatment of pellagra. When the patient's diet was restricted to large amounts of either autoclaved yeast or desiccated hog stomach, the oral lesions of pellagra healed rapidly. This suggests that there may be some etiologic relationship between pellagra and pernicious anemia. The evidence is too meager at the present time to justify the designation of vitamin G as the specific substance capable of curing pellagra. The oral manifestations of sixteen pellagra patients responded dramatically following the parenteral administration of massive doses of liver extract. The author suggests the use of large doses of liver extract, either intravenously or intramuscularly, whenever a patient severely affected has difficulty in ingesting or assimilating sufficient quantities of a highly nutritious diet.

Journal of Nervous and Mental Disease, New York

80: 253-376 (Sept.) 1934

*Acute Aseptic Meningitis. H. R. Viets, Boston, and J. W. Watts, Philadelphia.—p. 253.
Concerning Intraspinal Dermoids and Epidermoids: Report of Case. S. W. Gross, Cleveland.—p. 274.
*Treatment of Muscular Dystrophy with Gelatin. L. Stone, Topeka, Kan., and M. M. Abeles, New York.—p. 285.
Physical Dynamics of Encephalography. P. G. Schube, Boston.—p. 291.

Acute Aseptic Meningitis.—Patients having acute aseptic meningitis, described by Viets and Watts in 1929, have been reexamined and found to conform with Wallgren's description. Contrary to their opinion expressed in 1929, they now believe that the changes in the cerebrospinal fluid are not exclusively lymphocytic, although essentially so. Clots, also, may be found in the fluid. The most important point in differential diagnosis between this disease and tuberculous meningitis is the constantly normal sugar and chloride content of the cerebrospinal fluid in acute aseptic meningitis, contrary to the observations in tuberculosis. The disease should be considered a clinical entity, because no definite relationship has been shown to exist between it and any other diseases.

Treatment of Muscular Dystrophy with Gelatin.—Stone and Abeles used sheet gelatin in treating fifteen cases of muscular dystrophy and other similar disorders, as it is cheap and contains from 15 to 20 per cent of glycine. The gelatin, 100 Gm., was emulsified in orange or pineapple juice and given to the patient as a daily ration, to be taken at his convenience during twenty-four hours. The cases treated were of long standing, probably much less amenable to any form of therapy than incipient cases. Nine exhibited subjective sensory phenomena. Of these, five showed muscular dystrophy, one myasthenia gravis, one amyotrophic lateral sclerosis(?), one progressive muscular atrophy(?) and one chronic anterior poliomyelitis. Nine patients felt subjectively stronger to varying degrees. Eight showed an increase in muscular strength, omitting the myasthenic patient, who may have had a spontaneous remission. The changes varied in degree: they were all slight and two were altogether questionable. One myasthenic patient continued a downward course begun previously. Of the patients who improved objectively, five had muscular dystrophy, one had amyotrophic lateral sclerosis, one had progressive muscular atrophy(?) and one had chronic anterior poliomyelitis. The patient with amyotrophic lateral sclerosis (an advanced case) died six weeks after the discontinuance of treatment, his death being probably of bulbar origin. The authors believe the clinical phenomena sufficient to indicate that the substance has some therapeutic potency, which is possibly more marked in incipient cases. The therapeutic effect is probably due to the glycine content. The gelatin is bulky and unpalatable, and the results do not indicate superiority over pure glycine. Nevertheless, it might be the subject of further experiment in an effort to provide an inexpensive source of glycine. Beyond gastric discomfort and muscular dysesthesia there were no ill effects that could be attributed to the gelatin. The presence of sensory phenomena and even slight motor improvement in cases other than primary muscular dystrophy suggests that there may be similarities, perhaps identities, between the primary disorders of muscle metabolism and those of neurogenic origin, and that some aspects of the latter disorders may therefore be influenced favorably by glycine.

Kentucky Medical Journal, Bowling Green

32: 443-500 (Sept.) 1934

Report of Malpractice Suit. L. R. Curtis, Louisville.—p. 483.
Some Impressions of English Surgery Gained on Recent Visit. F. W. Rankin, Lexington.—p. 486.
Relation of Diet to Dental Caries. T. J. Marshall, Paducah.—p. 490.
Subtertian Malaria: Case Cured with Plasmochin. J. O. Nall, Princeton.—p. 492.
Insulin Treatment in Promotion of Gain in Weight. F. M. Stites, Louisville.—p. 493.
Why Like Begets Like. C. W. Reynolds, Covington.—p. 495.
Diaphragmatic Paralysis as Aid in Gastric Surgery. L. W. Frank, Louisville.—p. 497.

Maine Medical Journal, Portland

25: 175-202 (Sept.) 1934

Diseases of the Musical Profession. S. H. Kagan, Augusta.—p. 181.

Military Surgeon, Washington, D. C.

75: 113-196 (Sept.) 1934

Shell Fragment in Lung: Removal After Fifteen Years. H. Lilienthal.—p. 140.
*The Postmortem Roentgenogram. A. Bowen.—p. 145.
Technic for Subtotal Gastrectomy. F. H. Bowman.—p. 150.

Postmortem Roentgenograms.—Bowen points out that the postmortem roentgenogram is of great assistance when necropsy is not possible or desirable. In accident cases it will often reveal the cause of death and the extent of the injury. In cases of sudden death with thoracic symptoms it is often revealing, and in ordinary fatal medical and surgical cases it will demonstrate the terminal condition and give additional information as to the cause of death. In terminal accidents, such as spontaneous pneumothorax, hemorrhage from the heart, the lung or an aneurysm, pulmonary embolism or infarct, massive atelectasis or acute dilatation, a postmortem roentgenogram will show the condition. In a certain number of cases it will reveal as much as a necropsy examination and may be substituted for one. When late antemortem roentgenograms have been secured, they of course serve the same intent and purposes as the postmortem roentgenogram. Postmortem roentgenograms offer an important and instructive instrument for adding to the knowledge of the clinician, pathologist and roentgenologist.

New Jersey Medical Society Journal, Trenton

31: 439-496 (Aug.) 1934

Adult Tuberculosis in Children and Its Treatment by Compression Therapy. S. B. English and M. Gross, Glen Gardner.—p. 445.
Suppurative Hip in Children. G. H. Taylor, East Orange.—p. 458.
Lesions of Oral Mucosae. J. J. Eller and C. R. Rein, New York.—p. 461.
Roentgen Ray as an Aid in Obstetrics. L. J. Gelber, Newark.—p. 467.
Amebic Dysentery and the General Practitioner in New Jersey. M. Kraemer and M. Asher, Newark.—p. 469.
Urogenital Tuberculosis. S. L. Wang, New York.—p. 472.
Philosophy of Medical Service and Its Present-Day Applications. F. E. Elliott, Brooklyn.—p. 476.
West Coast Experiments in Providing Medical Service. S. A. Brumm, Philadelphia.—p. 478.
The Physician and Medical Economics. E. W. Sprague, Newark.—p. 483.

New York State Journal of Medicine, New York

34: 707-750 (Aug. 15) 1934

Recent Advances in Treatment of Epidemic Encephalitis. Josephine B. Neal, New York.—p. 707.
Five-Year Clinical Study of Prophylactic Value of Antirachitic Agents: Analysis of Nine Hundred and Forty-Eight Cases. A. G. De Sanctis and J. D. Craig, New York.—p. 712.
Bone Tumors and Allied Conditions. J. M. Hitzrot, New York.—p. 715.
Treatment of Acute Gonorrheal Urethritis in the Male. A. M. Crance, Geneva.—p. 725.
Treatment of Chronic Gonorrhea in the Male. E. M. Watson, Buffalo.—p. 728.
Gonorrhea in the Female. R. N. Ritchie, Rochester.—p. 731.
Minor Complaints of Pregnancy. C. J. Marshall, Binghamton.—p. 737.
Physical Therapy Department in a Hospital. F. E. Bauer, New York.—p. 741.

Ohio State Medical Journal, Columbus

30: 545-616 (Sept. 1) 1934

Toxemias of Early Pregnancy. W. D. Fullerton, Cleveland.—p. 565.
Diverticulosis: Diverticula of Alimentary Canal, Especially of Sigmoid Colon and Their Manifestations. E. H. Chapin, Columbus.—p. 569.
Electrocardiogram as Aid to Surgeon in Wounds of Heart. J. G. Brody, Youngstown.—p. 574.
Significance of Blood in Cerebrospinal Fluid. S. W. Gross, Cleveland.—p. 577.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

9: 201-266 (Aug.) 1934

Congenital Lung Cyst: Five Cases. G. B. Fleming.—p. 201.
Klippel-Feil Syndrome: Congenital Webbed Neck. H. S. Mitchell. —p. 213.
*Congenital Absence of Abdominal Muscles. L. G. Housden.—p. 219.
Glissonian Rickets. C. E. Kellett.—p. 233.
After History of Cases of Pleurisy with Serous Effusion in Children. D. W. Smithers.—p. 245.
Bone and Vegetable Broth. R. A. McCance, W. Sheldon and E. M. Widdowson.—p. 251.
*Acid Metabolism in Rheumatic Children. W. W. Payne.—p. 259.

Congenital Absence of Abdominal Muscles.—Housden reports a case of congenital absence of the abdominal muscles, presents the salient points of the thirty-three cases recorded previously and discusses the various views on the etiology of the condition. From this review he believes that the absence of the abdominal muscles is due to the atrophy of muscles formed previously, by pressure from an enormously dilated bladder and ureters, such pressure being probably increased by secondary ascites. The cause of the dilatation and hypertrophy of the bladder is considered to be an organic obstruction in the urethra, due no doubt to a neuromuscular incoordination (an achalasia of the vesico-urethral orifice) or to a definite organic obstruction.

Acid Metabolism in Rheumatic Children.—In an effort to determine whether there was a difference in the acid-base balance of the blood in the normal and the rheumatic child, Payne examined the urinary output of 200 rheumatic, asthmatic and normal children, respectively. The asthmatic group was chosen because at the time it was postulated that an element of alkalosis entered into the asthmatic syndrome. The observations show that the rheumatic child in a quiescent interval excretes more acid in its urine than does either an asthmatic or a normal child. Part of this excess of acid is due to organic acids. This excess production of acid is insufficient to disturb the equilibrium of the blood.

British Medical Journal, London

2: 291-338 (Aug. 18) 1934

Treatment of Lupus Vulgaris. S. Lomholt.—p. 291.
Eyes as Cause of Headache. A. Griffith.—p. 296.
Headaches in Relation to Ocular Conditions. W. Harris.—p. 298.
Reflex Asthma: Its Pathology and Treatment Including Review of Three Hundred and Thirty-Seven Cases. H. H. Moll.—p. 299.
Treatment of Bacterial Food Poisoning. G. R. McRobert.—p. 304.

Medical Journal of Australia, Sydney

2: 139-178 (Aug. 4) 1934

Toxic Goiter. A. H. À Court.—p. 139.
Id. G. Bell.—p. 144.
*Parasympathetic Nerve Supply to Distal Colon. H. C. Trumble.—p. 149.
The Fetish of Catgut. J. C. B. Allen.—p. 150.

2: 179-208 (Aug. 11) 1934

Causation and Treatment of Arthritis and Allied Conditions. H. Pern. —p. 179.
Paralytic Ileus. K. Ross.—p. 186.
Bacterial Flora of Mouths of Australian Venomous Snakes in Captivity. F. Eleanor Williams, Mavis Freeman and Eileen Kennedy.—p. 190.
Radon in Treatment of Cervical Carcinoma. W. G. Cuscaden.—p. 193.

Parasympathetic Nerve Supply to Distal Colon.—Trumble agrees with Telford and Stopford that nerve bundles do ascend in the hypogastric nerves from the pelvic nerves, but he maintains that these nerves do not represent the sole or main pathway for fibers of the pelvic nerves passing to the distal colon (excluding the rectum) and are merely the uppermost (probably) of a series of nerves supplying the intestine segmentally. They may be called the pelvic colonic nerves. The ascending pelvic colonic nerves do not enter the sympathetic perivascular plexuses, as a rule, but pass across these and enter the mesenteric border of the intestine direct and not in company with the vessels entering the intestine. They do, however, communicate with the perivascular plexuses. Often the uppermost nerves from the two sides do not unite but pass, one on each side of the inferior mesenteric artery and nerve plexus, to reach the colon.

Annales de Dermatologie et de Syphiligraphie, Paris

5: 649-744 (July) 1934

*Presence of Anticerebral Reagin in Cerebrospinal Fluid of Patients Having Dementia Paralytica and Tabes. R. Demanche.—p. 649.
*Urinary Elimination of Chlorides in Bullous and Vesicular Disorders of Skin. R. Zorn and P. Popchristoff.—p. 667.

Anticerebral Reagin in Cerebrospinal Fluid.—Demanche has made more than 1,000 comparative fixation reactions with an extract of brain and an extract of cardiac muscle, both on the cerebrospinal fluid and on the serum of patients suffering from various diseases. The myocardial antigen was an alcoholic extract of powdered heart previously extracted with ether and with 0.3 per cent cholesterol added. The cerebral antigen was an extract of human cerebral gray matter treated in the fresh pulp state without preliminary ether extraction in order to preserve the cerebral lipoids. The dry extract of both was 10.5 Gm. per liter. Their cholesterol content was 3.52 Gm. per liter for the cerebral extract and 4.16 Gm. per liter for the heart. The addition of cholesterol largely compensated the latter for the natural abundance of cholesterol in the nervous tissue. It was determined that the antigen had no anticomplementary power and that a similar testing of complement was applicable for both. The technic of the reactions was that of the author's modification of the Wassermann test. In order to study the results, the patients were divided into five groups: dementia paralytica, tabes, cerebrospinal syphilis comprising the different forms of secondary or tertiary meningo-encephalitis, nonsyphilitic disorders of the central nervous system, and generalized syphilis of different stages without characteristic nervous lesions. Analysis of the results indicated that the cerebrospinal fluid of patients having dementia paralytica and tabes possesses almost exclusively a special property of reacting in vitro with cerebral extracts. This reactivity is absent in all the other fluids and usually in the blood serum. Thus the group of parasyphilosis differs from other forms of nervous syphilis, and generally the cerebrospinal fluid from the blood serum. The author believes that the existence of these special anticerebral reagins confirms the doctrine of the local origin of the cerebrospinal reagins and brings a new argument in favor of the antigenic power of the organic lipoids and of the specificity of the cerebral lipoids. It also furnishes a supplementary procedure for the biologic diagnosis of parasyphilosis.

Elimination of Chlorides in Disorders of Skin.—Zorn and Popchristoff investigated the chloride metabolism in a number of patients with bullous and vesicular skin conditions. The amount of chloride usually ingested was 6.5 Gm. a day, though sometimes a diet containing from 10 to 12 Gm. was used. In every case it was felt that the chloride intake could be estimated within 0.5 Gm. limits. The method of Charpentier-Volhardt was used for determining the amount of chlorides in the urine. The results obtained from all patients in whom any doubt existed as to chloride intake, completeness of urine collections or other factors were discarded. In the one case of pemphigus satisfactorily studied there was a considerable chloride retention. They did not feel, however, that this was a cardinal etiologic phenomenon. In papulovesicular eczema an important chloride retention was observed in the majority of cases. By following these patients from day to day it seemed that this retention was accompanied by a juiciness of the affected cutaneous regions. They believe that the retained chlorides serve to form edema and the histologic sponginess that signifies eczema. In these cases of eczema in which it is not proper to speak of renal lesions, the formation of the edema practically coincides with the reestablishment of the elimination of chlorides.

Medicina Ibera, Madrid

2: 265-296 (Aug. 25) 1934

*Value of Vernes Test: Relation to Fixation of Complement Tests of Matefy, Daranyi and Fahreus. F. Diez Melchor.—p. 265.
Interlobular Pleurisy Opened into Bronchus: Case. L. Eizaguirre.—p. 276.

The Vernes Test.—Díez Melchor concludes that the fixation of the complement and the flocculation tests are the biologic methods most frequently resorted to for the diagnosis of the various forms of tuberculosis. The Vernes test is not specific, because it gives positive results in syphilis and in infections, and it gave negative results to the author in 16.94 per cent of the cases of proved tuberculosis. It has no diagnostic value.

The diagnosis of absence of tuberculosis based on the negative results of the test is more exact than that of its presence based on its positive results. The Vernes test has no relation to the anatomoclinical form of tuberculosis or to the extension of the lesions, but only to the degree of activity of the lesions. Hence its prognostic value. The highest figures of positive results of the test are given by the caseous and fibrocaseous forms in their period of evolution. The lowest figures of positive results and the large percentage of negative results of the test are given by the fibrous forms. The fixation of the complement is the only specific test for the diagnosis of tuberculosis. The results of the other reactions studied by the author (Matefy, Daranyi and Fahreus tests) were similar to those given by the Vernes test. These reactions are of physical nature showing only the presence of colloidal instability of the serum. The results of the Matefy and Daranyi tests absolutely lack diagnostic and prognostic value. The velocity of the sedimentation bears a close prognostic relation to the Vernes seroreaction.

Archiv für Gynäkologie, Berlin

157: 275-428 (July 20) 1934. Partial Index

Passage of Active Substance of Ergot into Milk of Nursing Mothers. P. I. Fomina.—p. 275.
Intestinal Motility During Puerperium. G. Halter and S. Simon.—p. 286.
*Uterovaginal Tamponade in Atonic Hemorrhages of Uterus. J. Kiss.—p. 315.
Criticism of Kielland's Operation for Prolapse. E. Weinzierl.—p. 332.
Atmocaustic Uterine Sterilization. L. Paullig.—p. 355.
Pneumonia in the New-Born. C. Müller and W. Bayer.—p. 372.
Experimental Studies on Detoxicating Function of Decidua. B. Szendi.—p. 389.
Luteinizing Granulosa Cell Tumor with Amenorrhea. R. Benda and E. J. Kraus.—p. 400.
*Special Position of Tubular Ovarian Blastomas (Arrhenoblastomas) as Regards Morphology and Hormone Function. H. O. Kleine.—p. 410.

Uterovaginal Tamponade in Atonic Hemorrhages of Uterus.—Kiss reports the experiences with Dührssen's uterovaginal tamponade in Hungary during the years 1931 and 1932. His report is based on 149 cases. This number amounts to 0.24 per cent of the total number of births. In general practice the method was resorted to in 0.03 per cent of the cases. The tamponade was nearly always made in the uterus and the vagina; once it was made only in the uterus and twice only in the vagina. In deciding on the tamponade, it was less the quantity of blood lost but rather the condition of the woman that was the determining factor. Tamponade was resorted to immediately in the clinics in only 5.7 per cent of the cases; in all other cases, less radical methods of hemostasis had been tried first; in private practice, tamponade was done at once in 28.08 per cent of the cases. The higher incidence of primary tamponade in the latter cases was due to the fact that there was no time left for trials with less radical methods. As to inspection of the uterus and removal of retained membranes, the author is of the opinion that it is advisable in institutions, where the intervention can be made with complete asepsis. Hemorrhages following placenta praevia were treated with tamponade in only 4 per cent of the cases. The mortality rate due to fatal hemorrhage amounted to 12.2 per cent in the material studied by the author. The danger of infection often credited to uterovaginal tamponade should be ascribed to previous intra-uterine interventions.

Special Position of Arrhenoblastomas.—Kleine points out that thirty-five cases of arrhenoblastomas of tubular structure have been reported thus far. Among the four cases that he observed was one in which there were dermoid cystomas in the other ovary. The growth of these tumors had begun at the hilus. Leydig's interstitial cells were demonstrable in all tumors. All patients exhibited more or less characteristic signs of virilism (psychic changes, altered body contours and changes in the hair growth and in the voice). In one patient the rete ovarii of the other ovary was considerably enlarged but was free from tumor cells. The development of a postoperative hyperthyroidism in one of the patients indicates the possibility of a pluriglandular disturbance. Reasoning along the lines suggested by R. Meyer, the author thinks that the parent tissues of the arrhenoblastomas are the rete ovarii, the medullary strands and the so-called extraglandular interstitial cells. These three epithelial formations represent heterosexual cell complexes of the ovary, which are present in small amounts in every ovary. The hypoplasia of the isosexual gonadal parenchyma seems to promote the development of the heterosexual tissues. The observations of other authors (R. Meyer) on younger women with arrhenoblastoma, in whom signs of virilism appeared simultaneously with the growth of the tumor, disappeared after extirpation and reappeared in case of relapse, prove a causal, incretory connection between these tumors and virilism. The author shows that three problems have yet to be solved: (1) the significance of the rete testis and of Leydig's interstitial cells for the development of the secondary male sex characters, (2) the problem whether arrhenoblastomas form a testicular incretion, and (3) whether there are relations between arrhenoblastomas and the suprarenal system.

Deutsches Archiv für klinische Medizin, Berlin

176: 455-566 (July 9) 1934. Partial Index

*Progressive Muscular Dystrophy: Its Heredity and Its Treatment with Glycine. S. Kostakow.—p. 467.
Investigations on Oxalic Acid Metabolism. A. Athanasiou and H. Reinwein.—p. 475.
*Localization of Cardiac Infarct by Means of Electrocardiogram. Jette Katz.—p. 480.
Intestinal Myiasis as Cause of Ulcerous Colitis Ending in Cure. G.-D. Koehler.—p. 491.
Microscopic Picture of Surface of Living Tongue. N. Henning and H. Becker.—p. 496.
Cause of Reduced Resistance of Diabetic Organism Against Infection. H. Horster.—p. 502.
Diagnosis of Bronchial Tumors. L. Hess and J. Faltitschek.—p. 510.
Influence of Nutrition on Metabolism During Work: Effects of Various Types of Protein. F. Bruman and O. Baumgartner.—p. 519.
Glycine Deficiency and Glycine Therapy in Progressive Muscular Dystrophy. W. Linneweh and F. Linneweh.—p. 526.
Determining Function of Liver by Tolerance Test with Insulin, Dextrose and Water: Blood Sugar Curves in Impairment of Liver. O. Gsell.—p. 532.

Progressive Muscular Dystrophy: Heredity and Treatment with Glycine.—Kostakow publishes a genealogical table with fifty-five members in three generations which reveals that fifteen of the descendants developed progressive muscular dystrophy and that all fifteen were boys. The girls remained healthy but transferred the disease to their sons. The six daughters of the first generation passed the disorder on to one or two of their sons, in all to 88 per cent of the males of the second generation. Seven women of the second generation, although themselves free from the disease, passed it on to six out of eight boys of the third generation. The children of the men, who had remained free from the disease, remained free from it through three generations. Thus progressive muscular dystrophy has a mode of heredity, in which the women transmit the disease although they themselves remain free from its symptoms; that is, the heredity is sex limited and recessive. A study of the cases of the successive generations revealed homology and homochronicity but no progressivity. The author discusses the value of glycine in the treatment of progressive muscular dystrophy. His observations were made in sixteen cases (fourteen from the genealogical table and two others). A tabular report of the results of the treatment indicates that the degree of improvement and the responsiveness of the disorder are dependent on the length and the progressiveness of the disorder but not on the age of the patient. The author gained the impression that the degree of improvement is proportional to the extent to which the muscles are still capable of reacting and inversely proportional to the progressiveness and the duration of the disorder. He rejects the statement that children with progressive muscular dystrophy are not at all or only slightly influenced by glycine, for his observations on seven children who improved greatly disprove this. He admits, however, that glycine is ineffective in cases with myasthenic components or with degenerative atrophies in syringomyelia, in spinal forms and in bulbar paralysis. Glycine treatment is indicated in pure myopathy and, to a certain extent, in cases in which on the basis of the clinical and electrical behavior serious impairment of the peripheral neuron can be excluded. He emphasizes that active patients require much larger quantities of glycine than do patients who rest.

Localization of Cardiac Infarct by Means of Electrocardiogram.—Katz points out that studies by Herrick, Smith, Pardee and others have made an electrocardiographic diagnosis of cardiac infarct possible. According to whether the characteristic sign, the reversion of the T wave, is found in the first

or in the third lead, Parkinson and Bedford differentiated two types of changes, T_1 and T_2. Later it was proved by Barnes and Whitten that this differentiation is of practical significance in that it permits an exact localization of the cardiac infarct. If the left coronary artery is occluded, the infarct is, as a rule, in the region of the apex of the heart, in the anterior wall of the left ventricle and in the anterior portion of the ventricular septum. The electrocardiogram reveals in these cases a reversion of the T wave in the first lead (type T_1). However, if a branch of the right coronary artery is obstructed, an infarct is nearly always in the posterior wall of the left ventricle and in the posterior third of the ventricular septum, and the electrocardiogram shows the characteristic changes, particularly the deep and pointed T wave in the second and third leads (type T_3). These observations have been corroborated by several investigators. The author observed in recent months two cases in which the localization that had been based on electrocardiography was corroborated by the necropsy. She gives detailed descriptions of these cases. One of them is especially noteworthy because the right ventricle was involved in the infarct formation, and this is rather a rare occurrence.

Klinische Wochenschrift, Berlin

13: 1137-1168 (Aug. 11) 1934. Partial Index

Serous Inflammation. H. Eppinger, J. Faltitschek, H. Kaunitz and H. Popper.—p. 1137.
*Significance of Ammonia Content of Blood for Estimation of Liver Function. J. Monguió and F. Krause.—p. 1142.
Microdemonstration of Several Volatile Amines and Their Influence on Permeability of Animal Membranes. A. von Wacek.—p. 1147.
*Experiences on Stability of Ergot Preparations. E. Rothlin.—p. 1148.
Etiology of Essential Hypertension and Eclampsia. M. Scheps.—p. 1151.
*Simple Roentgenologic Method for Exact Demonstration of Subnormal Length of One Leg. P. Bamberger and P. Zeitter.—p. 1153.

Ammonia Content of Blood in Estimation of Liver Diseases.—Monguió and Krause say that ammonia is produced in various functions of the organism. They give their attention mainly to the ammonia that is formed in the intestine and in the intermediate metabolism and enters the blood and then the liver, where the ammonium salts are changed into urea. Urea formation from the ammonium salts is one of the most important functions of the liver, for it prevents a sudden flooding of the organism with intoxicating ammonium ions. The amount of ammonium ions in the blood and in the tissue fluids must therefore present an indicator for the capacity of the liver to form urea. The authors found that the normal value of blood ammonia in human subjects varies between 0.028 and 0.06 mg. per hundred cubic centimeters of blood. They report their studies on normal dogs, on dogs with ligated choledochus and on dogs with Eck's fistula. They believe that their studies brought the experimental proof of Thannhauser's theory, who, like Fischler, considered poisoning due to the consumption of large amounts of meat an alkalotic condition produced by a flooding of the organism with ammonium ions. The aspects of chronic meat poisoning that developed in the dog with Eck's fistula, as well as the symptoms that developed after administration of urea and urease, justify the conclusion that a hyperammonemia is the cause of the vomiting and of the soporous state. For clinical and dietary procedures, these studies are important in that they indicate that in disturbances in which the parenchyma of the liver is impaired the protein intake should be curtailed as much as possible, while the carbohydrate intake is increased. Thus a method of treatment, which formerly had been adopted more or less intuitively, has now been given an experimental foundation.

Stability of Ergot Preparations.—Rothlin demonstrates that the stability of ergot preparations is rather limited. He sees the cause of this in the high sensitivity of the specifically active ergot alkaloids to air, light, alkaline reaction and high temperature. But in addition to these there must be still other as yet unknown factors, for even extracts that have been prepared and stored in the same manner show a different rapidity of disintegration. Tests revealed that even some of the pure extracts of ergot alkaloids have an insufficient stability. Ergotamine tartrate, however, was an exception, for it proved stable in controls extending over a period of twelve years. The histamine contained in ergot extract was found to disintegrate almost as rapidly as the alkaloids.

Roentgenologic Demonstration of Subnormal Length of Leg.—Bamberger and Zeitter point out that a difference in the length of the two legs is frequently the cause of an abnormal position of the pelvis and of the development of scoliosis. An exact determination of the difference in length is therefore highly important in orthopedic prophylaxis. The methods so far available lacked in exactness because it is difficult to feel through the skin the measuring points on the skeleton, and also because asymmetrical posture and restlessness on the part of the patient falsified the results. This induced the authors to devise a new method, which employs two wooden bars, one meter in length and marked with millimeter graduations. Each of these bars has two metal sliding pieces. The slides have a clamp that serves for the attachment of the roentgen casette and a securely fastened small metal indicator that projects from 3 to 4 cm. at a right angle over the edge of the measuring bars. The two bars are placed parallel on the roentgen table and to each slide is fastened a roentgen casette (9 : 12 cm.). The indicators should be approximately in the middle of the long side of the casette. The patient is placed in such a manner that the hip joints are above the middle of the upper casettes and the ankle joints on the two lower ones. It is advisable to make the distances of the slides the same on the two bars, since this prevents mistakes and also unnecessary calculations. The roentgen tube is at a distance of 1.5 meters and approximately above the knee joints. The four joints and the four slide indicators are photographed at one exposure, and the distance between the articular spaces (or other points on the femur or tibia) and their respective metal indicators are measured on the photographs. The sum of these distances left and right, respectively, reveals the difference in the length of the two extremities.

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127: 111-242 (July 24) 1934. Partial Index

*Biologically Active Substance in Tomatoes with Histamine-Like Action: Therapeutic Significance of Juices of Fresh Vegetables. F. Gleichmann.—p. 111.
*Clinical and Practical Significance of Determination of Diameter of Erythrocytes with Aid of Diffraction Method, with Especial Consideration of Diagnosis of Pernicious Anemia. H. R. Keller.—p. 132.
Trauma and Hypertension. W. Beiglböck.—p. 144.
Renal Rickets. R. Meier and E. Thoenes.—p. 149.
Gastric Hemorrhages and Anoxia of Cardiac Muscle. R. Aschenbrenner.—p. 160.
Diabetes and Hepatitis. H. Unger.—p. 166.
Clinical Contribution and Diagnosis of Myocardial Disturbances on Basis of Electrocardiographic Investigation. C. A. Bau.—p. 172.
Change of ST Interval in Electrocardiogram in Case of Postoperative Tetany. H. Marzahn.—p. 182.

Histamine-Like Action of Substance in Tomatoes.—The observation of certain circulatory manifestations in patients receiving a diet with large amounts of vegetable juices induced Gleichmann to search for substances with circulatory action in various vegetables. Traces of such substances were detected in carrots, potatoes and cabbage, but tomatoes contained substances with circulatory and secretory action in unusually high concentration. The author relates extensive experiments, which prove that tomatoes, ripe as well as green and fresh as well as canned, contain substances of intense biologic action. These substances are filtrable through a Berkefeld filter, have a high degree of thermostability and are resistant against digestion with hydrochloric acid pepsin. They have a tonicizing effect on the intestine, uterus, gallbladder and gastric muscles of guinea-pigs. Tests on dogs revealed that the biologically active substances contained in tomatoes promote the secretory action of the stomach by increasing the quantity as well as the acidity of the gastric juice. The substances increase also the secretion of pancreatic juice, but their effect on the secretion of bile is not quite clear. They produce a temporary reduction in blood pressure in atropinized as well as nonatropinized cats and rabbits. The diuresis is slightly increased by the tomato extract. Other problems, such as the decrease in blood pressure following intake of large amounts of the tomato extract into the gastro-intestinal tract, are still under investigation. Intracutaneous injections with the extract in human subjects reveals a tendency to wheal formation. The author is of the opinion that at least a part of the biologically active substances contained in tomatoes probably belong to the group of the histamine-like substances, but he considers it inadvisable to

identify them completely with histamine as long as the chemical proof has not been furnished. In a discussion of the clinical significance of the high content of tomatoes in histamine-like substances, he points out that the effects produced by diets providing large amounts of vegetable juices is probably largely due to their influence on the circulation, the vascular system and particularly the capillary apparatus. The efficacy of such diets in lupus, for instance, may be due to an improved blood perfusion. Moreover, the capillaries and precapillaries in a region of granulation and inflammation may be especially susceptible to small amounts of histamine-like substances. In this connection it is pointed out that under the influence of a vegetable diet abnormal capillary pictures frequently become more normal. The exclusion of the capillary obstructions effects an improvement in the regulation of the entire circulation, but particularly in the skin. This would also explain the efficacy of vegetable diets in capillaromotor disturbances, hypertension, migraine-like conditions, angiospastic angina pectoris, Quincke's edema and eczemas and other skin disorders, which are caused by capillary disturbances.

Determination of Diameter of Erythrocytes by Diffraction.—Keller points out that, although the enlargement of the mean diameter of the erythrocytes has been known for a long time as one of the most characteristic and persisting symptoms of pernicious anemia, it was of little practical significance because of the lack of a simple method. This deficiency was overcome when Pijper rediscovered the diffraction method. The author reviews the principle of Pijper's method, mentions several other investigators who employed diffraction, and finally describes his own observations in experiments with Bock's simplified and improved apparatus. In order to determine the normal limits of the diameter of erythrocytes, he examined 1,158 specimens and found that the normal diameter varies between 7.30 and 7.76 microns. He considers 7.60 microns the normal mean. The diameter showed no differences in the two sexes. In twenty patients with pernicious anemia, eighty-six specimens were examined, and it was found that even in case of considerable remission the mean diameter never went below the upper limits of normality. The author emphasizes that diffraction is simpler than the determination of the color index, and also probably more reliable. It proved helpful in the determination of the efficacy of a treatment. Macrocytoses not caused by pernicious anemia were detected in twenty-five cases of tuberculosis. However, the erythrocytic diameter reached only in one case the extent it has in an untreated case of pernicious anemia, and it was always possible to differentiate these macrocytoses from pernicious anemia by other methods. In cases of secondary anemia the mean diameter was either normal or below normal. Leukocytosis up to 150,000 did not interfere with the diffraction method, but when the leukocytosis reached 400,000 it became impossible.

Klinicheskaya Meditsina, Moscow

12: 953-1078 (May 26) 1934. Partial Index

Rule of Resultant State and Its Significance in Physiology and in Pathology. S. M. Leytes.—p. 954.
Tonsil Problem and Radiation Therapy. M. I. Karlin.—p. 976.
*Treatment of Cerebrospinal Meningitis by Spinal Punctures and Fractional Insufflation of Air. I. I. Matovetskiy.—p. 1011.
Cerebrospinal Meningitis in Young Children. V. Balaban and P. Krichevskaya.—p. 1014.
Climacteric Arthroses. G. G. Gambarov.—p. 1027.
*Rheumatic Infection of the Kidney. V. G. Palilov.—p. 1031.

Treatment of Cerebrospinal Meningitis by Spinal Punctures and Insufflation of Air.—Matovetskiy reports the results obtained in fifteen cases of acute epidemic cerebrospinal meningitis treated by the method of repeated spinal punctures followed by insufflation of air. From 25 to 30 cc. of the cerebrospinal fluid is removed and with the aid of a sterile syringe utilizing the same needle, from 10 to 15 cc. of air is slowly introduced. This procedure is repeated after two or three minutes. In young children smaller amounts are removed and correspondingly smaller amounts of air are introduced. The puncture is repeated every other day, daily in severe cases, and is kept up until the fluid becomes clear and on examination shows a normal albumin content and normal morphologic elements. During the introduction of air, patients complain of a backache and a pain along the vertebral column. The headache becomes aggravated. This, however, is followed from two to three hours later by a fall in temperature, remission of headache and an improvement in the general state. Of the fifteen patients thus treated, eleven got well and showed no sequels in a follow-up study from one to two years later. Of the four fatal cases, one was admitted with symptoms of vagus involvement, one exhibited a meningococcic bacteremia, two had a positive Queckenstedt sign, and the last exhibited xanthochromia of the spinal fluid. Results were always better when the treatment was instituted early. The author theorizes that the beneficial effect of insufflation of air is due to the washing out and forcing out of the infected fluid. The air, as it becomes warmer, rises into the subarachnoid space and displaces the fluid, which now may be removed by the secondary aspiration. The treatment may have the important effect of preventing formation of adhesions in the subarachnoid and spinal spaces. These adhesions may lead to a secondary hydrocephalus and to formation of encapsulated foci. The latter explain fatal exacerbations in apparently recovered patients.

Rheumatic Infection of the Kidney.—In histopathologic studies of seventy-five cases of rheumatic infection, Palilov found the existence of a diffuse glomerulonephritis in 16.2 per cent. He considers this alteration a specific manifestation of the rheumatic infection constituting, by its clinical course, a distinct cardiorenal type. Among rheumatic disorders of the kidney, the diffuse vascular alterations in the form of glomerulonephritis predominate over focal infections. The renal tissue is affected from the inception of the rheumatic process along with other organs and systems. The cardiorenal form occurs with greater frequency in older patients, those past 35, while the cardiac type without renal involvement is more frequent in younger patients. Renal involvement takes place in both the benign and the malignant types of rheumatic infection. It is apparently an identical process in the two. The course of the renal involvement is in most cases chronic, with a tendency to exacerbations in the form of acute glomerulonephritis. The chronic infection may be of a progressive character leading ultimately to renal insufficiency and uremic coma. Involvement of the kidneys aggravates the general course of the disease. The mortality in the author's material was 24.4 per cent during the first year for the cardiorenal type, as contrasted with 9.5 per cent for the cardiac type. The arterial blood pressure was found to be higher than in the cardiac form, but seldom as high as in nonrheumatic renal disease. The characteristic tendency to hypotonia is likewise manifested in the cardiorenal form of the rheumatic infection.

Bibliotek for Læger, Copenhagen

126: 327-382 (Aug.) 1934

*Cytologic Review of Different Forms of Goiter, Compared with Clinical Cases. S. Franck.—p. 327.

Cytologic Review of Goiter.—Franck tabulates ninety-eight cases, consisting of forty-nine of exophthalmic goiter (thirty-three with preoperative iodine treatment), five of toxic and forty-four of simple colloid goiter, treated operatively from 1929 to 1931. In the cases of exophthalmic goiter there was constant marked enlargement of the Golgi apparatus, a phenomenon found only in milder degree in some instances of simple goiter. The possibility is suggested that anomalies in the relation between the thyroid gland and the pituitary body may be an important factor in the etiology of exophthalmic goiter.

Ugeskrift for Læger, Copenhagen

96: 913-936 (Aug. 23) 1934

Attempt at Modification of Intestinal Flora in Rats and Men: Acidophilus Milk. Orla-Jensen and O. Winther.—p. 913.
*Experimental Investigation of Amidopyrine as Cause of Agranulocytosis: Six New Fatal Cases. P. Plum.—p. 916.
Agranulocytosis Originating After Small Dose of Amidopyrine, with Recovery. O. Knudsen.—p. 923.

Amidopyrine as Cause of Agranulocytosis.—Plum says that amidopyrine has up till now apparently caused agranulocytosis only in patients over the age of 20. He considers it necessary henceforth to refrain from prescribing amidopyrine and preparations containing this substance for adults, except in certain cases, such as inoperable cancer. The fatal cases reported occurred after therapeutic use of amidopyrine.